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# REHABILITATION OF THE CARDIAC PATIENT

Herman K. Hellerstein, M.D.
and
Amasa B. Ford, M.D., Cleveland

*• The process of rehabilitation begins at the moment the patient is first stricken with his disease. The goal is the maximal attainment within the patient's capacities. In approximately 80% of cardiac patients the total program can be managed by the private physician; in others, a team approach and help from specialists is necessary. It is assumed that adequate attention has been given to medical therapy, rest, relief of pain, oxygen requirements, nutrition, and sedation. In addition, the patient's emotional problems must be dealt with. The period of passivity which is frequently required at first should be terminated as soon as possible. The periods of hospitalization and of convalescence at home are followed by a period of vocational readjustment, and each presents problems that can be solved on the basis of available facts. There has been no evidence that employment has aggravated the underlying disease in cardiac patients, and there have been no medicolegal compensation cases involved in the employment of such patients.*

This report describes an orderly plan for the rehabilitation of the patient with heart disease from the initial illness through convalescence to the return to the world of work. Although many disciplines (medical, psychiatric, vocational, social service, occupational therapy, and physical therapy) may be employed, the physician is the guiding force and cohesive influence throughout the total illness and treatment. We assume that treatment of the cardiac patient is directed to the whole patient and to the total illness.

The physician's responsibility is for the comprehensive management of the patient, that is, diagnosis, medical or surgical care, convalescence, rehabilitation, and work prescription. Each phase of care must enjoy the same status as that of the so-called scientific aspects of diagnosis and treatment. The practice of rehabilitation should not be below the dignity of the physician. He should derive as much satisfaction from helping an incontinent hemiplegic patient to get to the stage where he can get out of bed to care for his own needs or from returning a coronary patient to competitive industry in a proper job as from making the diagnosis of monocytic leukemia or from controlling a case of ventricular tachycardia.[1]

Rehabilitation of the patient with heart disease involves the same basic principles and problems as rehabilitation of patients with any other type of disease. The term rehabilitation is defined as a process by which a patient is returned realistically to his greatest physical, mental, social, vocational, and economic usefulness and, if employable, is provided an opportunity for gainful employment in a competitive industrial world.[2] Rehabilitation has also been called restorative medicine.

The process of rehabilitation begins the moment the patient is first stricken with the disease, or at least when he is over the acute illness, and extends to the time when he is free of pain and out of the life-endangering stage. The need for rehabilitation is considered to exist in all etiological groups, in all economic groups, and in mild, moderate, or severe cases. The greatest need for rehabilitation exists for the patient with a relatively mild or moderate case, who, in the opinion of Irvin,[3] has been most neglected. Rehabilitation of the cardiac patient in industry basically concerns patients with mild cases, since over 70% of cardiac patients in industry fall in classes 1 and 2 (New York Heart Association functional classification). Industry is apparently not aware of the ease and success in rehabilitating this large group of patients with mild cardiac conditions. While outstanding success has been attained in the rehabilitation of the few severely impaired patients, numerically the greatest need is in the patients with milder cases, among whom the success will be the greatest.

From the Department of Medicine, University Hospitals of Cleveland, and the School of Medicine, Western Reserve University.
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### Important Factors

The specific goals of rehabilitation for the individual patient are variable: for some merely to leave the hospital, for others to return to the world of society, and for others to return to competitive employment. Regardless of the goal, each patient is eligible for rehabilitation to his maximal attainment.

In approximately 80% of patients, the private physician can manage the total rehabilitation. The other patients need the benefit of other disciplines (psychiatric, social service, occupational therapy, physiotherapy, and vocational counseling) and a team approach.

*Nature and Course of Heart Disease.*—The type of heart disease, extent of structural involvement, natural course of the disease, and extent of functional impairment are of major importance. There is considerable variation in the course of a given patient's heart disease, although, in general, the prognosis is quite predictable but subject to natural variations and to modifications by new methods of therapy. As more is learned about the natural course of heart disease, the outlook becomes less unfavorable. Dock [4] has recently compared the outlook of myocardial infarction with that of lobar pneumonia and considers it to be good and subject to improvement by dietary and other types of therapy. The physician must know that spontaneous improvement does occur in a significant percentage of cases and that the course of heart disease is not necessarily downhill.

*Emotional Factors.*—In 46% of the patients studied at the Cleveland Work Classification Clinic, emotional factors were next in importance to the heart disease per se. Much of this emotional difficulty was based upon fear, anxiety, and tension states that developed in previously susceptible individuals. Even in the most stable patient the onset of heart disease is associated with periods of anxiety and depression. The fear of death is often accentuated by publicity in newspapers and other mediums devoted to heart disease and by the economic and social pressures attendant on the development of heart disease.

Emotional disability, however, often arises from the interrelationship of the patient and his doctor. The patient's role in the genesis of iatrogenic disability is considerable. There is often a purposeful or subconscious garbling or misinterpretation of the physician's remarks or attitudes to fulfill what the patient wishes to hear, a form of selective deafness or miscomprehension. Heart disease often provides a strengthening of the patient's pre-illness basic needs, for example, an excuse to withdraw or flee from life's demands. However, the physician's role may be more important. The physician may be unwittingly careless in his words, attitudes, and management and thus contribute to the disability. The physician may also be misinformed about the natural cause of heart disease or uninformed about the latest advances. He may restrict the patient unnecessarily or misinterpret laboratory procedures.

The physician's contribution to the emotional problems of heart disease may stem from secondary gains which the physician derives from the patient's continued disability. These secondary gains can be considered to be psychological, financial, or professional. Quite characteristically, anxious physicians have more anxious and desperate patients. What are the gains, conscious or subconscious, for the physician in creating anxiety and disability? Crepe hanging, ominous prognosis of death, and overdramatization of the illness and its possible variations often reflect the psychological need of the physician to exert his power over life and death. In other words, some physicians feel that, if they cannot prevent death, at least they can predict it with a flourish, often deriving great inward satisfaction from this.

The physician may consider the terms impairment and disability to be synonymous. Legally, total disability means the inability to resume a previous occupation. The misinformed physician may disable his cardiac patient unnecessarily because he is unaware that most such patients suffer only slight impairment, let alone disability. The physician should not embrace the popular idea that all patients with heart disease are to some extent incapacitated.

In a few cases, iatrogenic disability has a financial connotation. The more fearful the patient, the closer and more costly his medical care. Sprague [5] has suggested that in a few cases the continued disability of the patient is financially beneficial to the physician.

A different type of economic implication in medical overprotection rests on the fact that many physicians are fearful of returning the cardiac patient to work because a death claim might reflect on the physician's practice. Often, however, the physician overprotects the patient in response to the patient's anxiety and to the pressures from the patient and his family or employer. The gains may also be selfish in another way, that is, to further a favorite method of therapy. Fear of impending death has been used to persuade asymptomatic patients with certain types of heart disease to submit to costly experimental procedures, the usefulness of which has not yet been clinically established beyond a doubt.

*Vocational Factors.*—Vocational factors include age, race, previous training, literacy, educational background, work history and work performance, interest in hobbies, skill levels, and job opportunities. The problem of transportation may be of prime importance. The stresses of traveling to and from a job and the work involved in walking long distances to the place of employment may far exceed the energy expenditure required to perform the job. Taxing features on the job, such as noise, dust, lifting, and incentive production, may be most important in determining the employability of a person with heart disease.

Such other diseases of significance as diabetes mellitus, peptic ulcer, gallbladder disease, tuberculosis, arteriosclerosis, progeria, and neoplasm may complicate rehabilitation and prognosis.

### Management at Onset of and During Acute Illness

In the subsequent discussion it is assumed that adequate medical therapy is prescribed in all instances. The importance of rest, relief of pain, restoration of oxygen system, adequate nutrition, and sedation is

taken for granted. Specific therapeutic and rehabilitative measures must be planned in detail to fit the specific needs of the patient.

*During Acute Episode.*—During the treatment of the acute episode, it is important, in order to prevent future disability due to fear, that the physician present to the patient a positive attitude, both hopeful and realistic, based on the knowledge that most patients recover from acute episodes of myocardial infarction, pulmonary edema, and congestive failure. He must be able to restrict the patient's activity without constricting his ego, one of the most important tasks in rehabilitation.

*After Crisis.*—After the crisis is over, there is a need to explain the immediate and long-term prognosis to the patient and to his family. The patient will need help in accepting the fact of his heart disease. He should be informed in general terms of the plan of therapy and of the nature of his heart disease. A concerted effort should be made to help the patient develop some insight into his disease and to encourage a receptive mood for future rehabilitation. The rationale of such care as dietary control, cardiac medication, and use of diuretics should be presented to the patient in general physiological terms. A simple description of heart function is well within the grasp of most patients. During the process of explanation and education, a relatively optimistic attitude should be maintained. The patient should not be advised that it will be necessary for him to change his whole way of living. Nothing need be farther from the truth, since 76% of the patients studied in the Cleveland Work Classification Clinic return to the same vocational and occupational classification.

The physician should create an atmosphere to encourage the patient to talk, think, and act constructively about his illness and to participate actively in his own rehabilitation. The period of passivity, which is frequently required in the treatment of myocardial infarction and rheumatic disease, should be terminated as soon as possible. For the patient with coronary and hypertensive disease, enforced passivity is especially harmful, being the antithesis of his aggressive and dynamic personality.

After the initial impact subsides, the attending physician should explain to the patient that he has had a heart attack, which consists essentially of a period of temporary deprivation of blood supply to an area of the heart. The concept of collateral circulation and the process of muscle healing should be discussed. The rationale of temporary restriction of physical activity should be explained, and the great capacity of the heart to recover should be stressed. Articles dealing with the successful readjustment of other patients to their heart disease should be made available. If the patient has rheumatic heart disease, the nature of the rheumatic process, the importance and feasibility of controlling streptococcic infection, and rheumatic recurrences should be dealt with. If hypertension exists, the beneficial effects of rest periods, weight loss, sedation, tranquillity, and happiness should be considered.

*Hospital Convalescence.*—During the period of convalescence, which usually starts from the third to fifth day after hospital admission and ends approximately after three to four weeks in the hospital, the management of the patient differs from that of medical care which predominated during the first few days. Here the team is organized, and the team approach should be put into action.

Restrictions should be reasonable and individualized. For the first several weeks the cardiac patient should be protected against communication with disturbing visitors, business associates, and relatives. Business worries should be excluded or minimized whenever possible. The patient should not be allowed free access to a telephone or allowed to conduct his business from the hospital bed. Exception to these rules may be advisable, however. A few minutes of discussion with an employer or a business associate may alleviate the patient's anxieties. The use of tobacco and sexual intercourse should be forbidden during the first four to six weeks of the illness.

*Rest and Activity.*—The prescription for bed rest should be individualized, and bedfast invalidism should not be created. More complete bed rest and quiet may be required for the first three to four days for the patient with myocardial infarction than for the patient with acute rheumatic disease or the hypertensive patient with congestive heart failure. The patient should be in a comfortable position. The period of passivity should be as brief as possible. He should be encouraged not to lie motionless but to move actively from one side to another. If seriously ill, he may require assistance. He should be allowed to feed himself unless such exertion produces symptoms.

Exertion in the form of graded exercise, such as flexing of the extremities, deep breathing, shaving, physiotherapy, or occupational therapy, should be advised. Details of the bedside chair treatment and early ambulation have been presented elsewhere by others. Regardless of when the patient's activity is increased, the normalcy of the ill-effects of bed rest and the reaction of patients to exertion (tachycardia, slight dizziness, weakness, and anxiety) should be explained.

During the convalescent period the full impact of the illness on the patient often becomes suddenly apparent. Psychiatric effects of heart disease may suddenly appear in the form of anxiety, depression with anxiety, regression, paranoia, hypochondriasis, dependency, or denial of illness. Throughout the illness the emotional status of the patient should be continually reevaluated. The patient may conceive of himself as being more invalided than he really is. These misconceptions should be sought out and corrected. Usually superficial psychotherapy by the private physician suffices, but in approximately 10% of the cases psychiatric consultation may be required.

The social worker may play an important role at this time for patients in all economic strata by helping the patient to use community facilities and to delineate the nature of the economic and family pressures. If a patient's wife is young and if it is necessary

for her to seek gainful employment, provision may be required for the children to be cared for and for other adjustments in the home to be made.

The rehabilitation of a patient with heart disease may be modified by associated diseases, such as diabetes mellitus and renal involvement, and particularly by thromboembolic complications. The details of management and rehabilitation of a patient with thromboembolism and especially hemiplegia have been summarized elsewhere. The outlook of the hemiplegic patient is by no means as hopeless as previously believed.[1] The majority of such patients can achieve self-sufficiency in the activities of daily living, and many can be selectively placed in jobs.

## Convalescence at Home

The period of convalescence at home is variable in its duration and often is difficult to define. During this period, the ultimate goal is to increase the patient's activities gradually and safely. At the present time, the physician usually errs in the direction of excessive restriction and limitation.

*Diet.*—During the convalescence at home, dietary restrictions should be lightened, whenever possible, to a point that is bearable. The diet should be reasonable and practical and therapeutically indicated. Severe restriction of salt or truly low-fat, low-cholesterol diets should not be prescribed without proper therapeutic indications. Only patients with a demonstrated disturbance of cholesterol balance and fat metabolism should require such stringent diets. Unless there is a specific indication, mass prescription of restrictive, unpalatable diets is not advisable. The inability to follow such diets often produce considerable anxiety in the average cooperative patient. Actually, this anxiety may aggravate cardiac symptoms, thus interfering with the work adjustment period.

*Removal of Restrictions.*—An increase of activity allows more privileges and a methodical withdrawal of restraints. A positive attitude should be presented to the patient as to what is allowed rather than what is denied. A reasonable program would gradually allow the patient to eat more than one meal with his family and to extend his bathroom privileges and freedom about the home. The physician should encourage the patient to go up and down one flight of stairs once a day for a few days and then several times thereafter, at first slowly and later at a normal pace.

The beneficial effects of exercise upon the development of intercoronary collateral circulation has been experimentally demonstrated by Eckstein [6] and substantiated by clinical observation of the lower morbidity and lower mortality of physically active patients with coronary disease than those who are inactive.[7] After two or more weeks, short walks in the confines of the patient's home and yard, short diversional automobile rides, and later the driving of a car should be permitted. The patient should be allowed to increase his activities to the point of slight discomfort. The desire to return to the world of work should be nurtured by increasing the number of contacts with the outside world and helping the patient formulate work plans.

The restrictions on tobacco and physical activity, including sexual, should be lifted according to the individual case. The categorical denial of tobacco to all patients must be condemned vigorously, especially in patients to whom occasional moderate use of tobacco has significance. Most patients with heart disease can smoke moderately without apparent harm. Restriction of tobacco is probably warranted only if a patient is shown to have a sensitivity to nicotine and if significant peripheral vascular disease is present.

*Evaluation of Fitness.*—The fitness of the patient is reflected in his reaction to increased activity. It is important to recall the easy fatigability of a normal person who has been restricted to bed. There is a need for a dynamic approach in the evaluation of cardiovascular function. A profile of cardiac function is required in order to detect various types of failure of the circulation, i. e., blood pressure regulation, coronary circulation, myocardial failure, and failure of cardiac mechanism.

## Measurement of Cardiac Reserve

During the convalescence at home and the work adjustment period the physician is faced with the need to evaluate the patient's cardiovascular functional status. A careful medical history is the principal clinical criterion of cardiac reserve, but its usefulness is limited by its subjectivity. Simple objective criteria are available today to judge a patient's recovery and his readiness for work. A patient's ability to perform ordinary home activities without dyspnea, angina, or other symptoms should be related to the energy cost of the whole range of physical exertion of humans. Measurements of the energy cost of many activities of humans have been made and are readily available. An excellent report was recently published by Passmore and Durnin [8] to which many references will be made. The physician today must be aware of ergometry and ergonomics, i. e., processes for dealing with the measurement of the energy requirements of activity of humans. This is especially important in the case of the cardiac patient whose energy capacity may be impaired by the basic heart disease.

The energy cost of such basal activity as sitting or lying is approximately 1.25 calories per minute. The calorie equivalent of oxygen is 4.8 to 5.0 calories per liter, i. e., one liter of oxygen consumed equals 4.8 to 5.0 calories of heat production. Skilled athletes using large muscle masses at maximal exertion (running, skiing) can increase their energy expenditure to a maximum of 26.5 calories per minute, while the maximal output for untrained men is about 14 calories per minute.[8]

Müller and Franz [9] estimate that the endurance limit of regular daily work for normal subjects averages 5 calories per minute, but the majority of modern industrial jobs require average energy expenditure of half that rate or less. A patient convalescing from acute heart failure or a myocardial infarct who is able to wash, shave, and dress (approximately 3 calories per minute) and walk around the block (6.6 calories per minute) is in all probability expending as much energy at home as he would at work. Recognition on the part of the physician of the relatively high energy cost of

such simple ordinary activities will enable him to advise the patient to resume work without a fear of overtaxing the patient's heart.

An even more objective estimate of cardiac reserve may be obtained from the familiar Master two-step test. Recent studies in our laboratory have confirmed the sound physiological basis of this test, which imposes the same caloric work load on subjects of various ages and weights.[10] These studies also emphasize that by observing the recovery rate of pulse and blood pressure as well as the usual electrocardiographic changes the physician can obtain a more detailed profile of the patient's response to exercise. Pulse and blood pressure should both return to within 10 points of resting level by two minutes after exercise. If the patient can perform the exercise without symptoms, an abnormal pulse rate or blood pressure, or electrocardiographic changes, it is safe to recommend that he undertake most types of industrial employment. If abnormal responses are noted, he still may be able to perform an average job, since the step test requires an energy output of 8.5 calories per minute, which is much greater than the average demand of representative jobs and considerably greater than the peak demands of these jobs (see table).[11]

*Energy Expenditures, in Calories per Minute, During Typical Working Day for Thirty-six Persons with Heart Disease*

| Category | Av. | Peak |
|---|---|---|
| Less than 1 | | |
| Electronics tester | 0.79 | 0.98 |
| 1-1.5 | | |
| Laundry crib supervisor | 1.25 | 1.47 |
| Maintenance electrician | 1.26 | 2.87 |
| Gauge setter | 1.28 | 1.80 |
| Tool crib attendant | 1.40 | 2.68 |
| Painter | 1.41 | 2.67 |
| Foreman | 1.46 | 2.35 |
| 1.5-2 | | |
| Planning clerk | 1.68 | 2.01 |
| Supervisor | 1.71 | 2.22 |
| Boxmaker | 1.74 | 2.17 |
| Drill press operator | 1.77 | 2.02 |
| Foreman | 1.78 | 4.04 |
| Plant guard | 1.82 | 4.12 |
| Tool grinder | 1.84 | 2.23 |
| Shift foreman | 1.88 | 2.58 |
| Light assembler | 1.88 | 2.40 |
| Inspector | 1.92 | 3.72 |
| Assembler | 1.96 | 2.49 |
| Light assembler | 1.98 | 2.92 |
| Stock picker | 1.99 | 3.24 |
| 2-2.5 | | |
| Stock picker | 2.00 | 2.82 |
| Set-up burnishing press worker | 2.04 | 2.28 |
| Stub lathe operator | 2.07 | 2.74 |
| Millwright (maintenance) | 2.15 | 2.63 |
| Stamper | 2.15 | 4.31 |
| Maintenance supervisor | 2.18 | 3.77 |
| Scarfing machine operator | 2.26 | 3.26 |
| Drill press operator | 2.27 | 2.98 |
| Turret lathe operator | 2.28 | 2.78 |
| Matron | 2.36 | 4.11 |
| Clutch tester | 2.40 | 2.92 |
| 2.5-3 | | |
| Welder | 2.60 | 4.47 |
| Supervisor | 2.67 | 3.22 |
| Janitor | 2.69 | 4.29 |
| Fireman (boiler) | 2.75 | 6.72 |
| Over 3 | | |
| Stock picker | 3.05 | 4.39 |

An integrated picture of the patient's recovery and improving cardiac reserve can thus be obtained by any physician during the period of convalescence. A careful history and therapeutic and functional classification employing the New York Heart Association criteria become more meaningful in the light of energy expenditure data, since there is an agreement in over 75% of the cases between this therapeutic and functional classification and the fitness as determined by physiological testing.[12]

Jones [13] writes that Class 1 cardiac patients can do 4.0 to 6.6 calories of work per minute; class 2, 2.7 to 4.0 calories per minute; and class 3, 2.7 calories per minute or less. The usual laboratory criteria used to note the recovery from an acute cardiac illness, such as temperature, erythrocytic sedimentation rate, transaminase levels, and electrocardiogram, provide further guideposts. Finally, the response of the blood pressure, pulse rate, and electrocardiogram to the measured stress of the Master two-step test provides a scientific estimate of cardiac reserve.

## Work Adjustment Phase

The decision that the patient may return to work initiates a new and critical phase of rehabilitation. In the absence of work classification units or rehabilitation services, the principles of a multidisciplinary approach can nevertheless be employed successfully by the private physician in most communities. Ideally a team should be used, consisting essentially of the private physician, industrial physician, employer (personnel manager or foreman), vocational counselor, and social worker. These individuals are united in an effort to match the patient's total capacity with the demands of the specific job.

Industrial job evaluation considers four aspects: (1) skill, (2) effort, (3) working conditions, and (4) responsibility. To the cardiac patient, effort and working conditions are of primary significance, although emotional factors, which include reaction to responsibility, are also important.

The effort required by a great many of the possible occupations in America nowadays is surprisingly small and not significantly greater than that required by ordinary home activities. Little wonder that many cardiac patients prefer to work than to remain at home. Reference has been made to the growing body of information available regarding the energy costs of various activities.[8] Our experience with 1,100 patients of the Work Classification Clinic of the Cleveland Area Heart Society and our current on-the-job studies [11] confirm the fact that actually cardiac patients, observed under actual working conditions and followed clinically over six years, are working at a wide variety of jobs without evidence of undue physiological stress.

A specific job description should be obtained by the vocational counselor and confirmed by the personnel manager or other representatives of the employer. The concept of the standard job is of no use, because there are so many variations in the requirements of the same job in a plant or in different plants in the same industry. The pattern of energy expenditure is apt to be more important than the magnitude. The frequency of rest periods, pauses, and relief of boredom are important factors. Our comparative studies of normal subjects and cardiac patients show that the same job performed by men of the same age and same skill re-

quire approximately the same energy. Energy expenditures vary more on the basis of personality needs of the worker than on the basis of energy requirements of the job.

Often a simple adjustment or job modification can be made in order to eliminate a single peak energy load which would make the job otherwise impossible. For example, a fellow-worker might tighten a lathe chuck or lift heavy parts in place for the worker with cardiac disease. A brief conference with the employer or union steward may make it possible for a relatively simple change in working conditions to be made which would make a job more suitable.

Observations of cardiac patients at work [11] demonstrate that in many jobs walking constitutes much the heaviest and most sustained exertion and that a rough estimate of the total energy requirements of a job may be obtained from the amount of walking involved. The estimation of the total energy requirements must include the energy expended in extracurricular activities, in travel to and from work, and the total work energy requirements of the job itself.

### Fatigue

Fatigue is a problem which is just being defined at present, and no good measurement of it is available. Studies to date, however, indicate that the psychological factors are predominant over simple energy expenditure, particularly at the level of exertion which might be considered for a worker with a cardiac condition.

Working conditions, in the sense of physical environment, may be of great importance in individual cases. A given energy expenditure will be much more stressful to the cardiovascular system under conditions of excessive heat than under normal conditions. Fortunately, however, heat and humidity control are being applied throughout all industry, including the proverbially inclement steel industry. Modern industrial physicians no longer think primarily in terms of "cardiac jobs." It is becoming increasingly evident that all but jobs requiring severe physical exertion (over 6 calories per minute) may be, or may be easily made, suitable for the majority of cardiac patients.

The emotional milieu of the job may be more important than its energy requirements to the patient with angina or other conditions with recognized emotional facets. Here the social worker may play a key role in recognizing the importance of the status of the job and the stress imposed by an overdemanding employer, by the pressure of competition in a piecework job, or by the patient's having accepted responsibility for which he feels unfit. Although the influence of the economic and family pressures generated at home may prevail during the working hours, more commonly the opposite pertains, viz., many patients have their attacks of angina only at home and not at work. It should be emphasized, however, that in almost all cases the satisfaction, restoration of self-respect, and relief of financial worry, which are the result of the return to work, outweigh any detrimental emotional stress associated with a job. A suitable job thus must provide status, self-esteem, and remuneration and be within the patient's present and future capacity.

After the emotional and physical factors are considered, the patient often cannot be returned to his previous occupation. This occurred in 24% of the cardiac patients studied in the Cleveland Work Classification Clinic. If job modification cannot be effected on a local level or selective placement obtained, the private physician may be forced to enlist the help of other disciplines, particularly vocational counseling and testing services and rehabilitation and placement services.

### Comment

The physician today finds himself burdened with cares which seem far removed from the "pure" domain of scientific medicine. Indeed it is fortunate that the cardiovascular capacity of the cardiac patient is so great and the energy requirements of industry so low that the physician does not have a greater percentage of patients who require the multidisciplinary approach. In approximately 42 cities in the United States today there are special work classification clinics, which relieve the private physician of these responsibilities in difficult cases. These clinics, supported by the American Heart Association, have proved their value in demonstrating that a person with heart disease can work safely in a variety of jobs.

We have already referred to our experience in the Cleveland Work Classification Clinic with 1,100 patients in the past six years. The team approach, with the team consisting of the medical social worker, vocational counselor, and cardiologist, has been employed successfully. Workers with representative heart disease have been studied, and results of the studies have fortified many of the concepts presented earlier. From the complexity of the needs of patients with heart disease, which include vocational guidance, vocational rehabilitation, physical rehabilitation, interpretation, and reassurance, it would seem that the nonintegrated approach would be unsuccessful in most of the above-mentioned cases and that the final management of the majority of such cases by one physician alone would have been inadequate. As mentioned before, the emotional problems are important. In 46% of the cases, the emotional impact of the illness on the patient was more important than the organic heart disease itself.

Follow-up studies have confirmed the practical value of selective placement of cardiac patients in industry. There have been no medicolegal compensation cases involved in the employment of such patients. There has been no evidence that employment has aggravated the underlying heart disease. In the experience of several work classification clinics, 70 to 75% of the cardiac patients have improved or remained unchanged while working. Follow-up studies have revealed that of the original group who were unemployed at the time of the first visit 60% were subsequently employed. The clinic team approach has enabled persons with heart disease to return to the status of wage earners, to gain selective placement, to obtain new jobs, to work safely in a variety of occupations and industries, and to adjust more satisfactorily to their heart disease.

## Summary

The factors important in the rehabilitation of the patient with heart disease include (1) nature and course of heart disease, (2) emotional reaction, (3) iatrogenic disability, (4) vocational features, and (5) presence of other diseases. In the management of such a patient, the need to prevent iatrogenic disability and cardiac neurosis and to expedite physical and emotional rehabilitation is important. Measurement of the patient's functional capacity in physiological and ergonomic terms is valuable in the regulation of the rate of rehabilitation and in matching the patient's capacity with the demands of specific jobs.


2065 Adelbert Rd. (6) (Dr. Hellerstein).

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# PROBLEMS OF RETAINED AND RECURRENT COMMON BILE DUCT STONES

**Seth W. Smith, M.D., Charles Engel, M.D., Beryl Averbook, M.D.**
**and**
**William P. Longmire Jr., M.D., Los Angeles**


*• A series of 1,381 initial biliary tract operations for calculous disease has been analyzed with respect to stones that escape detection during operation or form de novo after operation. The two kinds are often indistinguishable, and both are referred to as "retained stone." After 224 cholecystectomies with choledocholithotomy there were 14 cases of retained stone; after 1,156 cholecystectomies without choledochotomy there were only 9 cases of retained stone. Once the diagnosis of retained stone is established with reasonable certainty, reexploration is generally indicated. In this series, 22 patients underwent a second operation and four underwent a third. The unfortunate occurrence of retained stone is thus more frequently encountered after previous choledocholithotomy and the presence of a biliary duct stone indicates a possible source of serious difficulty.*


Although the problem of retained and recurrent stones in the common bile duct has received considerable attention over the years and although many excellent studies have been reported by Johnston, Waugh, and Good,[1] Glenn,[2] Buxton and Burk,[3] Cole,[4] Paine and Firme,[5] McKittrick and Wilson,[6] and others, the management of these difficult cases still poses a serious problem to the individual surgeon when he is faced with evidence of continued abnormality within the common duct after surgery on the biliary tract.

The decision as to whether a stone detected in the biliary ducts after surgery is retained or recurrent is in some cases an arbitrary one. Of the 24 patients in this study, in 15 the stones were definitely retained, and in 4 they were felt to be recurrent on the basis of long symptomatic intervals involved; the type of stones in the remaining 5 could not be determined with any degree of certainty. Consequently, in the interest of simplification, no effort is made in the following report, except in certain instances, to continue the distinction between retained and recurrent stones, and thus they will be loosely referred to as "retained."

From the Department of Surgery, University of California Medical Center, and Wadsworth General Hospital, Veterans Administration Center, Los Angeles, and Los Angeles County Harbor General Hospital, Torrance, Calif.

Read in the Panel Discussion on Common Duct Stones before the Section on Surgery, General and Abdominal, at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

The reported incidences of gallbladder and biliary duct stones in the population at large are somewhat variable. On the basis of 16,936 autopsies of individuals of all ages, performed at the Mayo Clinic between 1910 and 1942, Robertson and Dochat [7] reported a 16.3% incidence of gallstones; 12.6% of 10,587 men and 22.6% of 6,349 women had gallstones. Glenn [2a] states that a safe estimate of the incidence of gallstones would be at least 10% for the general population of the United States and 20% for the population over the age of 40 years. Stones in the gallbladder

increase in incidence with the passage of years, showing a considerable rise in the 35-to-55-year group. Robertson and Dochat [7] found that 22.3% of women and 9.7% of men in the fourth decade had gallstones. In persons over the age of 55, the increase progresses less sharply, but it is estimated that one out of three individuals will have gallstones at the age of 75. The incidence of common duct stones also increases with advancing age, and autopsy records indicate that one-third to one-half of individuals over the age of 80 years with cholelithiasis will be found to have biliary duct stones. Such stones are infrequent, however, in individuals under 40 years of age.

After common duct exploration, with or without removal of stones, the incidence of retained stone has been reported by various authors to vary from 3 to 10%.[8] Few reports have appeared concerning the incidence of retained or overlooked stones after negative common duct explorations. Buxton and Burk [3] noted retained stones by postoperative cholangiograms in 9 (4%) of 249 persons who underwent negative choledochotomies; in 3 of these patients (1.2%), the stones were later removed surgically. Glenn [2b] performed follow-up studies of 3 to 18 years on a group of 100 patients who had cholecystectomy and choledochotomy. No stones had been found on primary exploration in 46 of these patients, but calculi were recovered from the biliary ducts in 2 of these 46 (4.2%) on reexploration.

TABLE 1.—*Incidence of Retained Stones After 1,381 Biliary Operations*

| First Operation | Total Patients, No. | Patients with Retained Stones, No. | Patients with Retained Stones, % |
|---|---|---|---|
| Cholecystectomy | 1,156 | 9* | 0.8 |
| Cholecystectomy with choledochotomy | 224 | 14† | |
| Choledochotomy only | 1 | 1 | 6.7 |
| Total | 1,381 | 24 | 1.7 |

* Found in one patient at autopsy.
† Second operation not yet performed on one patient. Diagnosis by cholangiogram.

The incidence of retained stones after choledocholithotomy has been reported by various authors to vary from 5.8 to 28% (table 8, below). As will be discussed more fully below, it would appear that the incidence of retained stones after choledocholithotomy performed by experienced surgeons would approximate 8 to 9%.

Finally, it is of interest that the incidence of retained stones or of stones discovered in the biliary ducts after cholecystectomy without biliary duct exploration is surprisingly low. Glenn [2b] followed up 100 consecutive patients who had had cholecystectomy more than 10 years prior to his study. Seven of these had symptoms leading to common duct exploration, and stones were found in four. Thus, an accurate incidence of 4% of retained stones after cholecystectomy is given.

## Case Material

*Initial Operations.*—A total of 1,381 initial biliary tract operations for calculous disease has been reviewed (table 1). These cases are collected from the records of three hospitals: the Wadsworth General Hospital, Veterans Administration Center, Los Angeles; the Los Angeles County Harbor General Hospital, Torrance; and the University of California Hospital, Los Angeles, for the period from Jan. 1, 1947, to March 1, 1956, inclusive.

TABLE 2.—*Incidence of Retained Stones After Choledochotomy With and Without Removal of Stone*

| | Total Patients, No. | Total Patients, % | Patients with Retained Stone, No. | Patients with Retained Stone, % |
|---|---|---|---|---|
| Stone removed | 123 | 55 | 14 | 11.0 |
| No stone found | 102 | 45 | 1* | 0.98 |
| Total | 225 | | 15 | |

* It is not known whether the stone is retained or recurrent in this case.

The various incidences of retained stones in this study are inaccurate because of certain inadequacies of follow-up. Some patients have not been followed up for a long time, especially those who have undergone second and third operations, and others have been lost to follow-up. Furthermore, an undetermined number with retained stone undoubtedly went elsewhere for their second operation. The group of six patients with retained stones in the University Hospital, however, were of this itinerant nature, having had their first operation performed at hospitals other than one of the three included in this study. Thus, to an undetermined extent, this elusive factor would tend to be balanced.

Except in the University Hospital, the bulk of the operations were performed by surgical residents. Twenty-four instances of retained (and recurrent) stones occurring subsequent to the first biliary operation were found, representing 1.7% of the total. Nine of the 24 followed 1,156 cholecystectomies (0.8%) and 15 followed 225 common duct explorations, associated with cholecystectomy in all but one case, an incidence of 6.7% (table 1). Of the total of 225 patients who underwent choledochotomy, 123 (55%) had stones removed and in 102 (45%) no stones were found (table 2). There were 15 instances of retained stones after cholodochotomy: 14 after previous choledocholithotomy (11%) and one after negative common duct exploration (0.98%).

TABLE 3.—*Incidence of Retained Stones After Second Operation*

| Second Operation, Type | No. Patients, | Patients with Retained Stones After Second Operation, No. | Patients with Retained Stones After Second Operation, % |
|---|---|---|---|
| Choledochotomy | 20* | 5† | 25 |
| Choledochotomy with choledochoduodenostomy | 1 | 0 | 0 |
| Choledochotomy with choledochoplasty | 1 | 1‡ | (100) |
| Total | 22 | 6 | 27.2 |

* In 9 of these patients initial operation was cholecystectomy.
† Retained stones found at autopsy in 2 patients.
‡ Stricture present, possibly due to stone.

Of the 24 patients with retained stones, 12 were female and 12 male. With the group of 10 males at the Veterans Administration Hospital excluded,

there were 12 females and 2 males. The age of the 24 patients varied from 26 to 76 years, with a median age of 62.

*Second Operations.*—As shown in table 3, a second operation, consisting of common duct exploration, was performed on 22 of the 24 patients with retained stones. Retained stones were diagnosed by autopsy in one of the other two patients and by a postoperative cholangiogram in the other, who has not yet undergone a repeat operation. Common duct exploration was repeated in 13 of the 22 patients undergoing repeat operation. In the remaining nine patients, however, the initial operation was cholecystectomy; hence, common duct exploration, the second procedure, was performed for the first time. In addition to common duct exploration, one patient had a cholecystoduodenostomy and another a choledochoplasty.

*Third Operation.*—Twice-retained stones occurred in six patients, or 27.2% of those requiring a second operation. In two of the six patients the stones were found at autopsy, while four patients underwent a third operation (table 4). Of these four patients, all are progressing well except one (case 1), who had multiple intrahepatic stones and in whom an operative cholangiogram indicated possible further retained stones. In another, the gallbladder was removed at the third common duct exploration.

A total of 26 second and third operations were thus necessary in the 24 patients with retained or recurrent stones, and one patient may require a fourth operation. The operation performed was common duct exploration in all instances. This was combined with choledochoduodenostomy in one case, with choledochoplasty in two, and with cholecystectomy in one. Because of the recurrent status of some of the stones for which second and third operations were necessary, the incidences of true retained stones are altered. This factor is analyzed in greater detail in the Comment, below.

## Cholangiography

*Operative Cholangiography.*—Operative cholangiography was used in only three instances in connection with the 24 patients of this series. Its use in the total of 225 common duct explorations has not been determined. Although not yet a routine procedure, it has been performed with increasing frequency within the last two to three years covered by this study, but not sufficiently to be evaluated in this report.

TABLE 4.—*Patients upon Whom Three Operative Procedures Were Performed Because of Retained Stones*

| Case No. | Operation | | |
|---|---|---|---|
| | 1st | 2nd | 3rd |
| 1 | Cholecystectomy | Choledochotomy | Choledochotomy* |
| 2 | Cholecystectomy | Choledochotomy | Choledochotomy |
| 3 | Cholecystectomy | Choledochoplasty (stricture, possibly due to stone) | Choledochoplasty (stricture due to stone) |
| 4 | Choledochotomy | Choledochotomy | Choledochotomy and cholecystectomy |

* This patient may require still another choledochotomy.

*Postoperative Cholangiography.*—Cholangiography was performed postoperatively, with use of the inlying T-tube, in 29 instances (table 5). It was performed after initial common duct exploration in 12 patients; definite evidence of obstruction by retained stones was seen in 9 of them and dilated ducts in 2, and only one was reported as normal. The presence of retained stones was verified by common duct exploration in 11 and by autopsy in one. After a second common duct exploration, cholangiography was done in 15 patients; obstruction by stone was revealed in 2 and dilated biliary ducts in 3, and a "normal" reading was obtained in 10. The presence of retained stones was verified by subsequent common duct exploration in the two patients showing obstruction, and, at autopsy, two years later, stones were revealed in one of the patients with dilatation of the ducts. No further operations have been performed on the remaining two patients with dilated ducts or the 10 with normal cholangiographic findings. Two cholangiograms made after a third common duct exploration were read as normal. These data help to confirm the established value of the postoperative cholangiogram in the management of biliary stones.

TABLE 5.—*Relation of Findings on Postoperative Cholangiography and Subsequent Choledochotomy*

| Previous Operation | Patients, No. | Findings | | | Stone Verified by Choledochotomy |
|---|---|---|---|---|---|
| | | Obstruction | Dilated Ducts | Normal | |
| First | 12 | 9 | 2 | 1 | 12* |
| Second | 15 | 2 | 3 | 10 | 3* |
| Third | 2 | 0 | 0 | 2 | 0 |
| Total | 29 | 11 | 5 | 13 | 15 |

* Stone verified in one case by autopsy.

*Intravenous Cholangiography.*—Intravenous cholangiography was utilized eight times. Findings were normal in two patients. Stones were visualized in three patients and later identified by operation in two (one patient has not yet had a second operation). Retained stones were likewise later positively identified in one patient in whom there was nonvisualization of the ducts and in two patients with dilated biliary ducts but in whom no stones were seen on cholangiography. These data are meager and only support the observations by others that intravenous cholangiography, because of the effects of altered hepatic function and difficulty in visualizing the distal common duct, cannot positively indicate the absence of stones.[9]

## Biliary Fistula

In this series, persistent biliary fistula occurred three times. In one patient, a calculus was demonstrated at the ampulla of Vater by cholangiogram two weeks postoperatively; the T-tube was removed after three weeks, and a biliary fistula persisted until the stone was removed by a second common duct exploration two months later. In the second patient, fistula occurred two months after choledocholithotomy and two incisions and drainages of subhepatic abscesses. A small stone at the ampulla of Vater and many in the hepatic ducts were removed one month later, or three months after the initial operation. The third patient developed a biliary fistula after cholecystectomy. Stones were passed through this fistula for two and one-half years, and then it healed. After four years several stones were removed from the cystic duct

stump and from the common duct. This case supports the observation by Hicken and co-workers [10] that some biliary fistulas eventually heal even in the presence of retained calculi.

## Biliary Flush

Best's technique of biliary flush [11] was tried in four instances in an effort to remove stones definitely identified by cholangiogram. In no instance was it successful, all stones being removed eventually by choledocholithotomy.

TABLE 6.—*Incidence in Other Series of Retained Stones After Choledocholithotomy*

| Source | Period | Patients Undergoing Choledocholithotomy, Total No. | Patients with Retained Stone | |
|---|---|---|---|---|
| | | | No. | % |
| McKittrick and Wilson[6] | 1949 | 52 | 3 | 5.8 |
| Buxton and Burk[3] | 1934-1946 | 190 | 17 | 8.9 |
| Johnston, Waugh, and Good[1] | 1940-1950 | 153 | 12 | 8.0 |
| Glenn[2b] | 1932-1950 | 100* | 5 | 9.7 |
| Singleton and Coleman[13d] | 1950-1955 | 43 | 4 | 9.3 |
| Paine and Firme[5] | 1945-1953 | 206 | 57 | 28.0 |

* Group with 3-to-18-year follow-up.

## Comment

The data obtained from this study and from those of others shed light on two questions regarding the problem of the retained stone that concern the surgeon performing operations on the biliary tracts. 1. Are most retained stones overlooked because the common duct is not explored or are most of these overlooked during exploration? 2. Are the majority of retained stones overlooked during common duct exploration where stones were identified and removed, or are they overlooked and retained during explorations where no stones were found? In answer to the first question, as shown in table 1, the incidence in our study of retained stone was 0.8% after cholecystectomy alone but 6.7% after common duct exploration with or without identification and removal of stones. Although these percentages are probably lower than the absolute incidences because of inadequacies in follow-up, the ratio of one to the other is probably fairly accurate. In answer to the second question, in our series retained stones were found after choledocholithotomy in 11% and after common duct explorations where stones were not found in only 1%.

These data indicate that, if the surgeon explores biliary ducts, adhering to the accepted indications (palpable stone, dilated duct, thickened wall of the duct, gallbladder with small stones and large cystic duct, and a history of jaundice with pain), his chances of leaving stones in the unexplored duct after cholecystectomy alone are gratifyingly low. The incidence in our series of stones found in explored ducts is 55%, and in other published reports the incidence varies from 33% to 69%, with a rough average of around 50%.

These and other published data show that most stones are retained after choledocholithotomy, a clinically significant fact in that an individual harboring stones in his biliary ducts possesses a source of potentially serious difficulty. Operative experience and awareness of the problem presented by biliary duct stones would appear to affect significantly the incidence of retained stone after choledocholithotomy performed by any individual or group of surgeons; to some extent this is reflected in the published literature (table 6).

Neither our data nor those published in the literature, which is scant in this regard, allow the formulation of any sort of rule-of-thumb estimate as to how many patients undergoing a second operation for retained stones will require a third exploration for twice-retained stones. Our series (table 3) reveals that 6 of 22 patients, or 27.2%, still had retained stones after second operative procedures. Three of the 22 patients were operated on for recurrent stones and 5 for possible recurrent stones; hence, the corrected percentage of second operations for true retained stones would be 14%. Six patients still harbor stones in the common ducts after two previous operative procedures; in three of these patients stones were retained after attempted removal of probably recurrent stones and in three the stones were truly twice-retained. As the retained stones in two of the six patients were found at autopsy after death from unrelated causes, a third operation was necessary in only four (table 4). In this group of four, one patient, who originally had cholecystectomy alone, followed by two common duct explorations for large numbers of extrahepatic and intrahepatic stones in each instance, still has indications of thrice-retained stones, and a fourth operative procedure may be necessary in the future. These cases illustrate that it may be very difficult to rid a small percentage of patients of all biliary stones and emphasize the importance of the problem presented by intrahepatic stones. Norman [12] found that, of 46 patients with verified hepatic calculi, 31 also had stones in the intrahepatic ducts. It was impossible in 18 patients (in 14 of whom the stones were definitely intrahepatic) to remove all the hepatic stones visualized in cholangiograms made at operations. As a result, choledochotomy was repeated in 7 patients, and, finally, in 26 of the 46 patients, calculi were left in spite of choledochotomy. In his thorough study, Norman points out the value of operative cholangiography performed both before and after the duct is opened and stresses the importance of radiographic technique utilizing exposure of the plates at various angles in order to avoid superimposition of intrahepatic ducts on one another.

TABLE 7.—*Type of Stones Detected After Biliary Surgery*

| Initial Operation | Patients, No. | No. of Patients with | | |
|---|---|---|---|---|
| | | Retained Stones | Recurrent Stones | Stones of Undetermined Status |
| Cholecystectomy | 9 | 4 | 3 | 2 |
| Cholecystectomy and choledochotomy | 15 | 11 | 1 | 3 |
| | 24 | 15 | 4 | 5 |

The surgeon is also concerned with knowing how soon a retained stone will make itself evident if overlooked at the time of common duct exploration. Retained stones in 15 of the 24 patients in this series showed definite evidence of their retention early in the postoperative period. Three of the 15 patients had

persistent biliary fistulas; in 10, obstruction of the duct by calculi was demonstrated by postoperative cholangiogram; and in 6 significant symptoms were present postoperatively.

It is of interest that more stones that were believed to be recurrent were found after cholecystectomy alone than after cholecystectomy with common duct exploration (table 7).

This study confirms the value of the postoperative cholangiogram, which was performed in 29 instances (table 5). Obstruction was found in 11 instances and dilated ducts in 5; the presence of stones was subsequently verified by operation or autopsy in 15 of these 16 cases. The diagnostic accuracy of the postoperative cholangiogram, as indicated in this and in numerous other studies, is sufficient to indicate the advisability of using the T-tube after each common duct exploration for stone. Furthermore, the T-tube should not be removed until cholangiography has been done and the most accurate knowledge possible has been gained concerning the patency of the common duct.

The surgeon is also interested in knowing whether a retained stone should be immediately removed surgically or whether and to what extent watchful waiting or nonoperative methods, such as biliary flush, will result in passage of the calculus. Johnston, Waugh, and Good [1] saw 12 patients with residual common duct stones, diagnosed by postoperative cholangiograms in 11 and by symptoms in one, and found a second operation to be necessary in only 6. Evidence of stone subsided in five, and the remaining patient died and did not come to autopsy. The data in our series are inadequate to indicate definite answers to these questions. Twenty-two of our 24 patients with retained stones eventually had stones removed at a second operation; retained stone was diagnosed at autopsy in one of the remaining 2, and in the other a second operation has not yet been carried out. In 9 of the 22 patients the interval before the second operation was from 18 months to 33 years, and during these periods these patients experienced asymptomatic intervals, some of many months' duration. Difficulties related to the biliary tract continued to reappear, however, until all stones were removed. These results suggest that, once the diagnosis of retained or recurrent common duct stone is established with reasonable certainty, common duct exploration without delay is generally indicated.

Although our use of Best's method of biliary flush [11] was unsuccessful in the four instances in which it was tried, other authors [13] had had varying degrees of success with his method and with that of Pribram.[13c] Glenn [2a] states that he has abandoned the use of the latter method because of reactions and delayed cholangitis that followed the use of the solvents advocated. Singleton and Coleman [13d] recently reported that "most authorities have found no harmful effects" from the use of chloroform and ether and point out the importance of agitating the stone by irrigation to effect its dissolution. It would appear that success with these methods depends in large part upon the degree of patience exerted by the user and also on the fortitude of the patient and his desire to avoid another operation.

## Summary

Twenty-four of 1,381 patients had retained or recurrent common duct stones after operations for calculous biliary disease. The incidence of retained and recurrent stone after cholecystectomy appears to be 4% or less. This percentage is apparently due to the liberal exploration of the common duct by most surgeons, who have adhered to the indications currently recommended. The incidence of retained and recurrent stone after all common duct explorations appears to be in the range of 3 to 10%; after negative explorations, it is approximately 4%, but after previous choledocholithotomy by experienced surgeons, the incidence appears to be about 8 to 9%. The unfortunate occurrence of retained stone is thus more frequently encountered after previous choledocholithotomy, indicating that the presence of biliary duct stones per se may be the major source of serious difficulty for the patient (and the surgeon).

In our series of 24 patients with retained and recurrent stones, 22 underwent a second operation, 4 underwent a third operative procedure, and one may require a fourth operation, illustrating the difficulty of finally ridding a small percentage of patients of biliary duct stones. Due to the fact that operative cholangiography has been employed by us only in the latter part of the period studied, its value cannot be accurately evaluated. Use of the postoperative cholangiogram was sufficient to confirm the value of this procedure. The T-tube should be used after each choledochotomy and should not be removed until at least one postoperative cholangiogram has been obtained. Our study indicates that difficulties related to the biliary tract continued to reappear until all stones were removed surgically. Therefore, once the diagnosis of retained or recurrent common duct stones is established with reasonable certainty, reexploration is generally indicated.

Dr. William C. Boeck Jr., of the Los Angeles County Harbor General Hospital, aided in the collection of material for this report.

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# PRACTICAL VALUE OF OPERATIVE CHOLANGIOGRAPHY

C. Allen Wall, M.D.
and
S. Patrick Peartree, M.D., St. Louis

• *Cholangiography can be performed during operations on the biliary system by injecting the contrast medium through the cystic duct before exploring the common duct or by injecting through the T-tube after exploration. The film is exposed during a brief period of apnea induced by the anesthesiologist, and while the film is developed the gallbladder can be removed. Cholangiograms with sodium acetrizoate as the contrast medium were made in 444 patients. The common duct was explored in 231, and calculi were recovered from the ducts in 115. Stones missed on operative exploration were detected by operative cholangiography in 36 patients. Postoperative complications have occurred, and both false-positive and false-negative results have been noted. These difficulties can be reduced by attention to details, and the usefulness of the results has been demonstrated.*

It is self-evident that the best way to manage stones within the extrahepatic biliary ducts is to recognize their presence and remove them.[1] It is our purpose to discuss the role of operative cholangiography in furthering this objective.

The subject of operative cholangiography is a controversial one. The controversy revolves around the accuracy of the technique in relation to the alleged disadvantages of its use.[2] Certain questions arise: Does this additional diagnostic adjunct enhance the thoroughness of an operative exploration of the ducts? Will a more general adoption of this procedure reduce the number of unnecessary common duct explorations? Is the additional inconvenience justified by the results obtained? These are pertinent questions attending the use of this procedure to which our data will be applied.

Our observations are drawn from an experience with operative cholangiography in 444 patients. In this presentation only certain practical observations derived from the data are presented. A more detailed analysis is presented elsewhere.[3]

## Case Material

Four hundred forty-four patients were subjected to operative cholangiography during the past four years. These patients were drawn from the surgical services of the St. Louis University Hospitals; more than four-fifths of the procedures were performed by the resident staff. In 57%, cholangiography was performed through the cystic duct prior to exploration. In 32%, the common duct was explored and contrast medium injected through the T-tube after exploration. In 11%, both preexploratory and postexploratory operative cholangiograms were done. The common duct was explored in 52% of the 444 patients. Calculi were recovered from the ducts in half of the explorations (26%).

From the departments of surgery and radiology, St. Louis University. Dr. Wall is now with the Department of Surgery, Walter Reed Army Institute of Research, Washington, D. C.

Read in the Panel Discussion on Common Duct Stones before the Section on Surgery, General and Abdominal, at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

## Technique

The standardized technique used in this series is diagrammatically illustrated in the figure. Certain points may be emphasized. Wound drapes should be sutured to the skin, and all radiopaque sponges and instruments must be removed from the right upper quadrant before injection of the agent. The absence of bubbles in the system is insured by aspiration of bile into the syringe. We have used with satisfaction a 70% aqueous solution of sodium acetrizoate, injected in increments of 5, 5, and 10 ml., with exposure of a film after each injection. It is important to inject slowly to avoid raising the intraductal pressure.

The need for cooperation between the surgeon, anesthesiologist, and radiologist has often been stressed. After injection of the contrast medium, the anesthesiologist induces a state of apnea and instructs the technician to expose the film. During the short period while the films are being developed, the gallbladder may be removed. With proper teamwork there is minimal prolongation of the operating time.

### Indications for Operative Cholangiography

Operative cholangiography may be helpful in two sets of circumstances. First, after either a positive or a negative operative exploration of the common duct, it may serve as additional insurance against retained stones. Second, when the indications for exploration are questionable, the operative cholangiogram may help to solve the surgeon's dilemma. If stones are demonstrated by cholangiography, exploration is mandatory. If the cholangiogram is negative, the surgeon may refrain from opening the duct with greater assurance that stones are not being overlooked.

In this series the reasons for the use of operative cholangiography were as follows. In a small number of patients (17%), the procedure was used to help evaluate the method. In more than four-fifths of the patients, it was felt that operative cholangiography would be a useful adjunct in reducing the incidence of overlooked common duct stones. Thus, operative cholangiography was performed to insure against retained stones in 42% of the patients (after positive exploration in 22% and negative exploration in 20%) and to avoid unnecessary exploration of the duct in 41%.

In certain instances one is compelled to explore the common duct. When there is palpable stone, a dilated or thickened common duct, bile containing particulate matter, or an acalculous gallbladder in the presence of typical biliary colic, as well as in certain types of jaundice, the indications for exploration are clear-cut. However, in selected patients with a history of jaundice or pancreatitis and with no operative evidence of common duct obstruction, the indications for exploration are less clear. Moreover, exploration of the common duct in every patient with multiple small stones in the gallbladder would result in a number of needless explorations. In such instances the surgeon may be undecided whether to open the duct. Under these circumstances, what help may be expected from operative cholangiography? A review of our own experience sheds light on this question.

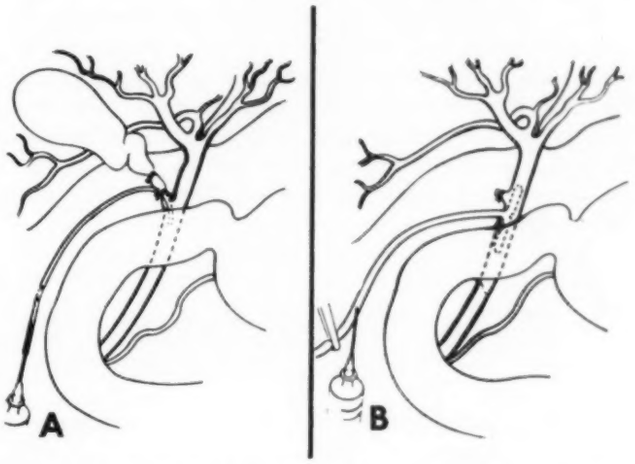
The over-all diagnostic accuracy of the method in these 444 patients was 88%. This relatively high figure is an index of the attention directed to technical precision, which is so important in obtaining satisfactory cholangiograms. In 63 patients (14%) stones were seen on the operative cholangiogram. In 36 of these 63 patients, the common duct had been explored and judged to be free of stones. In these 36 patients, the retained stones lay within the common duct in 24 instances and within the hepatic ducts in 12. In all but two patients (both with hepatic duct calculi), the stones demonstrated on operative cholangiography were removed on immediate reexploration of the duct. In the two patients with stones in the hepatic ducts, repeated efforts at extraction were unsuccessful. Delayed cholangiograms during the postoperative period revealed that the stones in both instances had dropped from the hepatic radicle into the common duct; both were removed at a second operation.

In evaluating the usefulness of this procedure, one must consider whether the additional time, expense, and inconvenience of operative cholangiography in 444 patients was justified in order to remove stones that would otherwise have been retained in 34 patients. Certainly some of these patients would have required a second operation for removal. In those who were spared a second procedure because of operative cholangiography, there is no doubt as to its merit.

In 144 patients with questionable indications for exploration but with no direct evidence at operation of a stone within the duct, the decision against common duct exploration was abetted by a negative operative cholangiogram. Such a decision is always open to question until complete, long-term follow-up establishes its correctness.

### Problems Encountered

The method was judged to be unsatisfactory in 12% of the patients in this series. More than half (6.5%) of these poor results were due to errors in technical performance. These errors included poor positioning of the patient, motion during exposure of the film, interposition of opaque objects, extravasation of the contrast medium, and faulty radiographic technique.




Technique used for operative cholangiography, *A*, before exploration and, *B*, after exploration.

The remaining unsatisfactory results were due to errors in interpretation of the films, with 3.5% false-positive and 2% false-negative.

It is useful to review some of the more common reasons why a surgeon may be misled by the cholangiogram into searching for a "stone" that does not exist. These false-positive results are occasioned by incomplete filling of the hepatic ducts, spasm of the ampulla preventing the inflow of contrast medium into the duodenum, and the presence of air within the ducts. Additional sources of error are the end of the polythene catheter or the limbs of the T-tube, which may simulate a stone by pressure against the wall of ducts or when they are viewed on end. Space does not permit a discussion of certain simple precautions that will prevent these errors.

In addition to the false-positive cholangiograms, one may have false-negative results, in which small stones are masked by the contrast agent. This occurred in nine of our patients (2%). In eight instances, the stones measured 5 mm. or less. They were demonstrated by subsequent exploration or delayed cholangi-

ography. It is reasonable to conclude that this 2% represents a minimum figure for false-negative results, since certain undetected stones, masked by the contrast medium, undoubtedly later pass into the intestine.

As with any technical procedure, certain complications may be anticipated. These include a mild, transient low-grade fever during the immediate postoperative period, presumably due to regurgitation of the medium into the blood stream, and a transitory elevation of the serum amylase level, possibly correlated with the not infrequent reflux into the pancreatic duct. Some degree of extravasation occurred in 13% without apparent untoward effects.

### Comment

From the review of our data it is apparent that satisfactory results can be obtained with operative cholangiography by careful attention to certain technical details. The widespread use of delayed cholangiography after surgical exploration and T-tube decompression of the common duct indicates that the principle of radiologic confirmation of the absence of stones within the ducts is generally accepted.

Those surgeons who employ delayed cholangiography but rarely use operative cholangiography must agree with the principle of operative cholangiography but avoid the procedure because of dissatisfaction due to errors in technique and interpretation. With increased care in technical performance, these errors can be reduced and the procedure should come into wider use.


### Summary

We have performed operative cholangiography in 444 patients subjected to biliary tract surgery, with a diagnostic accuracy of 88%. Stones missed on operative exploration were detected by operative cholangiography in 36 patients. Reasons for the unsatisfactory results include poor technique and false-negative and false-positive cholangiograms. Increased attention to details of technical performance is necessary. With the resultant improvement in operative cholangiograms, there should be more widespread use of the method.


Walter Reed Army Institute of Research, Washington 12, D. C. (Dr. Wall).

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# DISAPPEARANCE OF "STONE" SHADOWS IN POSTOPERATIVE CHOLANGIOGRAMS

Warren H. Cole, M.D.
and
William H. Harridge, M.D., Chicago


*• The possibility that stones in the common bile duct may disappear during conservative treatment with 3 to 4 Gm. of bile salts per day by mouth is illustrated by the histories of nine patients selected from a larger series of patients who have undergone cholecystectomy and choledochostomy with insertion of a T-tube in the common duct. The nine patients constituted a group in whom postoperative cholangiography gave evidence of retained or recurrent stones and in whom obstruction of bile flow was incomplete so that the T-tube could be clamped all the time. In seven of these patients, the "stone" shadows vanished in 8 to 13 weeks. In two, the shadows persisted, and stones were removed at a subsequent operation. Proof that the shadows represented stones and that the administration of bile salts played a decisive part in their disappearance was not absolute, and the question whether the stones disintegrated, dissolved, or passed unchanged was not settled, but significant evidence relating to these problems was obtained.*


During the past seven years we have encountered nine patients in the Illinois Research and Educational Hospitals who after cholecystectomy and choledochostomy had residual "stones" in the common duct as determined by cholangiography. All except one of these had been operated on in our own hospital. Under conservative treatment, consisting of prolonged T-tube drainage and administration of bile salts (3 to 4 Gm. per day in divided doses), dissolution, disintegration, or passage of these "stones" was observed in seven of the nine cases. We should add that we have no proof that these shadows represent stones; all we can say is that they resemble those cast by stones.

From the Department of Surgery, University of Illinois, College of Medicine, and the Illinois Research and Educational Hospitals.

Read in the Panel Discussion on Common Duct Stones before the Section on Surgery, General and Abdominal, at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

### Evidence Supporting Theory of Dissolution or Disintegration of Stones

In addition to the clinical data presented herein, we wish to present other evidence supporting the possibility that the stones dissolved or disintegrated. The fact that the "stone" shadows disappeared rapidly rather than by slow decrease in size suggests that the stones disintegrated rather than dissolved, unless they were passed through the sphincter of Oddi. Most of the shadows were so large that it hardly seems possible that the stones could have been passed. Disintegration might take place by dissolution of the outer "hard" portion and of the matrix holding the cholesterol together; in this case, they might crumble and be passed as granular debris. All surgeons have seen many stones so soft that they broke into amorphous fragments as they were removed from the common duct. It is barely possible that a disturbance in the cholesterol–bile salt ratio, as suggested years ago by Andrews,[1] might exert a prominent influence in the "dissolution."

It is a well-known fact that, if gallstones from humans are placed in the gallbladder of a dog, the stones will disappear in a few weeks or months. It is rather obvious that this disappearance is related to dissolution and not to passage through the small cystic duct of the dog. The increased bile salt content in the dog's bile, as reported by Sobotka [2] and others, could readily explain this disappearance by dissolution in the dog.

The great variation in the percentage of common ducts explored, as noted in the literature, offers fairly good evidence that a huge number of stones in the common duct are passed or dissolve. McKittrick and Wilson [3] report the performance of cholecystectomy and choledochostomy in 100 consecutive patients with stones in the gallbladder, with stones found in the common duct in 52%. Cattell [4] reports exploration of the duct in 45.7% of 1,104 patients having cholecystectomy, with stones found in 16.8% of the entire group. On the other hand, Glenn [5] reports opening the common duct in only 10.5% of 2,472 patients having cholecystectomy, with the finding of stones in only 7.2% of the entire group. Recognizing the vast difference in discovery of stones, as listed above, Glenn followed up 100 consecutive patients who had undergone cholecystectomy performed by his group more than 10 years previous to his study. Of these 100 patients, 93 were asymptomatic; 7 had symptoms leading to common duct exploration, but stones were found in only 4 of these. If we add this 4% to Glenn's original figure of 7.2, we obtain a figure of only 11.2%, which is still below Cattell's figure of 16.8%. It appears that the stones were probably present in many of Glenn's patients not having a common duct exploration. If so, they must have been passed or "dissolved."

One might ask the question, why should stones disintegrate in the common duct after cholecystectomy, whereas they grow and perhaps occasionally form in the common duct of patients not having had their gallbladder removed? There may be a possible explanation in the fact that, with the gallbladder in place, a certain amount of concentration of bile takes place, although this is less so in diseased gallbladders. If concentrated bile is expelled from the gallbladder, flowing over stones in the common duct, one might expect growth of the stone and not dissolution, particularly if the diseased gallbladder absorbs bile salts, with disturbance of the bile salt–cholesterol ratio, as claimed by Andrews.[1]

If disintegration of stones does take place in the common duct after cholecystectomy, one would not expect it in patients having complete obstruction of the duct, because the possible effect of dissolution by constant flow would be obliterated. In all seven of our patients in whom there was disappearance of the "stone" shadow we were able to clamp the T-tube constantly, although in two patients jaundice persisted for a prolonged period; in one patient, clamping of the T-tube was associated with leakage of considerable amounts of bile around the T-tube.

*Findings in Seven Patients in Whom "Stone" Shadows Disappeared*

| | Surgery | | | No. of Wk. Postoperatively for Cholangiogram | | | | No. of Wk. Postoperatively Bile Salt Therapy Begun |
|---|---|---|---|---|---|---|---|---|
| Case No. | Date | Jaundice | Stones Found in Common Duct | 1st | 2nd | 3rd | 4th | |
| 1(fig. 1) | 6-15-55 | No, but history | None | 4, stone | 9, stone | 16, stone | 25, normal | 8 |
| 2 | 6-14-49 | Yes | Many | 7, stone | 12, stone | 21, normal | ... | 12 |
| 3 | 1-7-52 | Yes | None | 11, stone | 12, stone | 15, normal | ... | 11 |
| 4(fig. 2) | 11-12-54 | Yes | 2 | 2, stone | 7, stone | 11, stone | 18, stone (5th study at 31 wk. normal) | 2 |
| 5 | 1-5-53 | Yes | Yes | 2, stone | 7, normal | 9, normal | ... | 2½ |
| 6(fig. 3) | 7-1-54 | No, but history | Yes | 2, stone | 5, stone | 10, stone | 15, normal | 2 |
| 7 | 1-29-54 | Yes | None | 3, stone | 8, normal | ... | ... | 2 |

### Analysis of Cases

As stated, during the last seven years we have found "stone" shadows in the postoperative cholangiograms of nine patients in our hospital who have had cholecystectomy and choledochostomy. In seven, the shadows disappeared, but in two, in whom the T-tube was kept in place for a year, the shadows remained; operation was performed on these two patients after this interval, and stones were found in the common duct. We advised operation in one patient at the end of six months, but he declined because of urgent business; in the other patient operation was delayed because the patient was lost to follow-up and did not return. Treatment in all cases was confined to the oral administration of bile salts (3 to 4 Gm. per day in divided doses) and constant clamping of the T-tube. We would not attempt this treatment if the duct were completely obstructed.

The table reveals the important data for each patient as related to operation, cholangiograms, and therapy. The history and other clinical findings are

given in the case reports, below. In all cases the shadow or deformity was demonstrable in more than one film. Several cholangiograms in other patients, not reported on, revealed deformities, but in most cases a diagnosis of air bubbles could be made quite readily. In two others, the shadows were doubtful and were absent in a subsequent cholangiogram. These, too, might have been stones, but we did not include them since there was definite doubt about the identity of the shadows. The time required before a normal cholangiogram was secured was 25, 21, 15, 31, 7, 15, and 8 weeks respectively. The shadow might have been absent at an earlier date, but we made no attempt to obtain weekly cholangiograms. At least we know that the shadow persisted through 16, 12, 12, 18, and 10 weeks, respectively, in five of the seven patients. In two of the patients the "stone" shadows were present in four and three different cholangiograms, respectively, spaced three to seven weeks apart.

Obviously, we cannot prove that the shadows revealed in the cholangiograms were stones. However, since the deformity was present in more than one film in all cases and fulfilled the roentgenographic requirements for stones, we feel the diagnosis of stone was justified. Perhaps the most diagnostic shadows are those with irregular shape and surface surrounded completely by iodopyracet (Diodrast) compound. A concave shape on the terminal end of the cholangiographic shadow is considered fairly conclusive of stone.

Although we gave bile salts (3 to 4 Gm. per day in divided doses) to all patients, we have no evidence whatsoever that this drug played a vital role in the disappearance of the shadows. However, we are sufficiently convinced of its efficacy that we gave it to all, and we will continue to do so until we have evidence to the contrary. It is true that, in two cases, bile salt therapy was short (see last column in the table).

We have additional evidence that all seven patients had stones in the common duct, inasmuch as five had jaundice at the time of operation and two had a history of jaundice. It is also very significant that in three of the seven patients no stones were found in the common duct at the time of choledochostomy; two of these three had jaundice at the time of operation and the third had a history of jaundice. Because of lack of space the cholangiograms of only three of the patients are reproduced here.

## Report of Cases

Case 1.—A 56-year-old woman came to the hospital in June, 1955, complaining of recurrent attacks of pain in the right upper quadrant with jaundice. However, at the time of admission she did not have jaundice and had not had any pain for two or three weeks. She was operated on on June 15, 1955. The gallbladder contained numerous stones and was buried rather deeply in the liver. The cystic duct was large in diameter but short. The common duct was explored with a common duct scoop, but no stones were found. The scoop passed through the sphincter of Oddi without difficulty. A cholangiogram, performed while the patient was on the table, revealed no shadow suggestive of stones; iodopyracet entered the duodenum readily. Accordingly, it was assumed (probably erroneously) that the stone causing the attacks of jaundice might have passed through the sphincter of Oddi into the duodenum. The common duct was closed around a T-tube and the wound closed. A postoperative cholangiogram was taken July 12, 1955 (four weeks postoperatively). There was moderate dilatation of the common duct, and a shadow typical of that of a stone was noted at the ampulla of the common duct (fig. 1). In spite of the obstruction noted on the x-ray, apparently bile did pass into the duodenum readily, because the T-tube was clamped almost continuously after June 27, 1955. In August, the patient was placed on bile salt therapy, receiving 1 Gm. four times a day. Cholangiograms taken Aug. 19 and Oct. 10, 1955, revealed an obstruction similar to the one noted on July 12. However, the cholangiogram

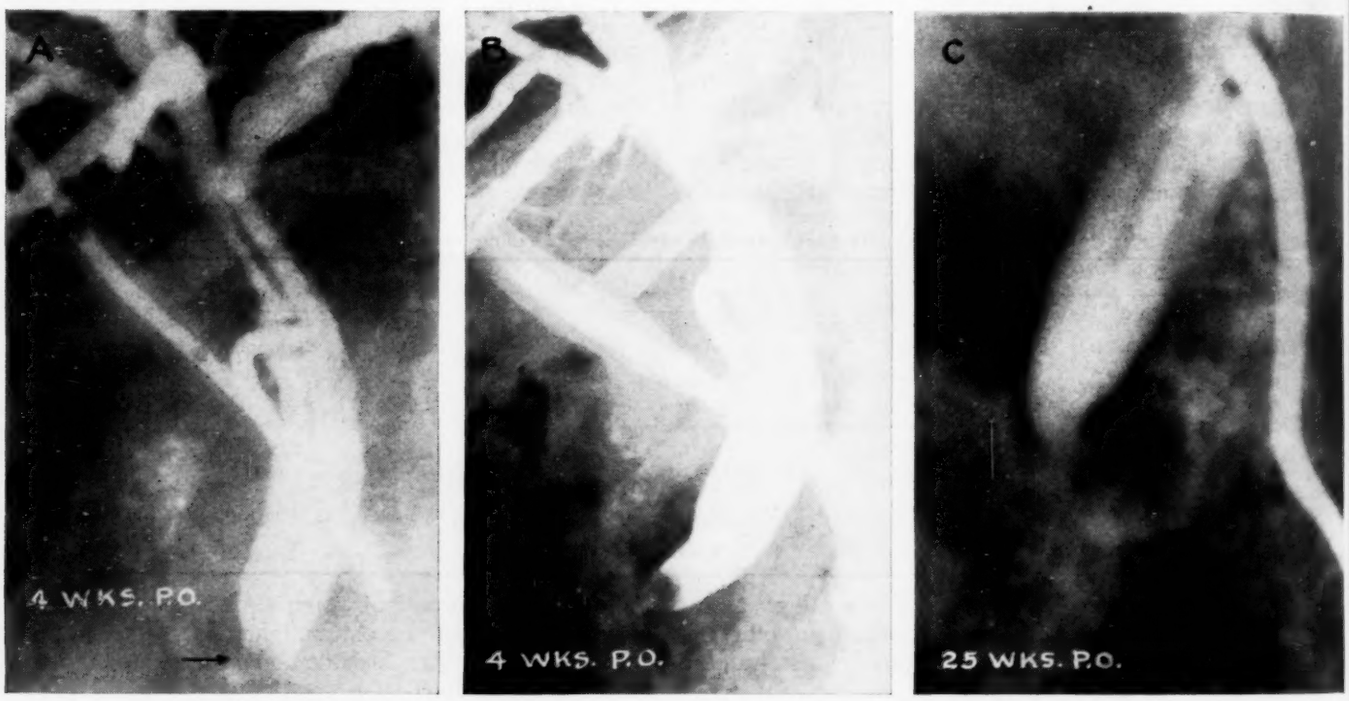


Fig. 1 (case 1).—*A* and *B*, different views of cholangiogram (four weeks postoperatively), revealing "stone" at ampulla. Later cholangiograms taken 9 and 16 weeks postoperatively (not shown here) confirmed presence of stone but revealed slight decrease in common duct size and better drainage of dye into duodenum. *C*, normal cholangiogram, taken 25 weeks after operation.

taken Dec. 6, 1955 (25 weeks postoperatively), revealed no obstruction, and iodopyracet entered the duodenum readily. The T-tube was removed Dec. 14, 1955. When last seen, six months later, the patient was asymptomatic and had no pain or recurrence of jaundice.

CASE 2.—A 48-year-old woman with diabetes was admitted in early June, 1949, complaining primarily of vomiting and slight abdominal distress. However, shortly after admission, she developed severe pain in the right upper quadrant and jaundice.

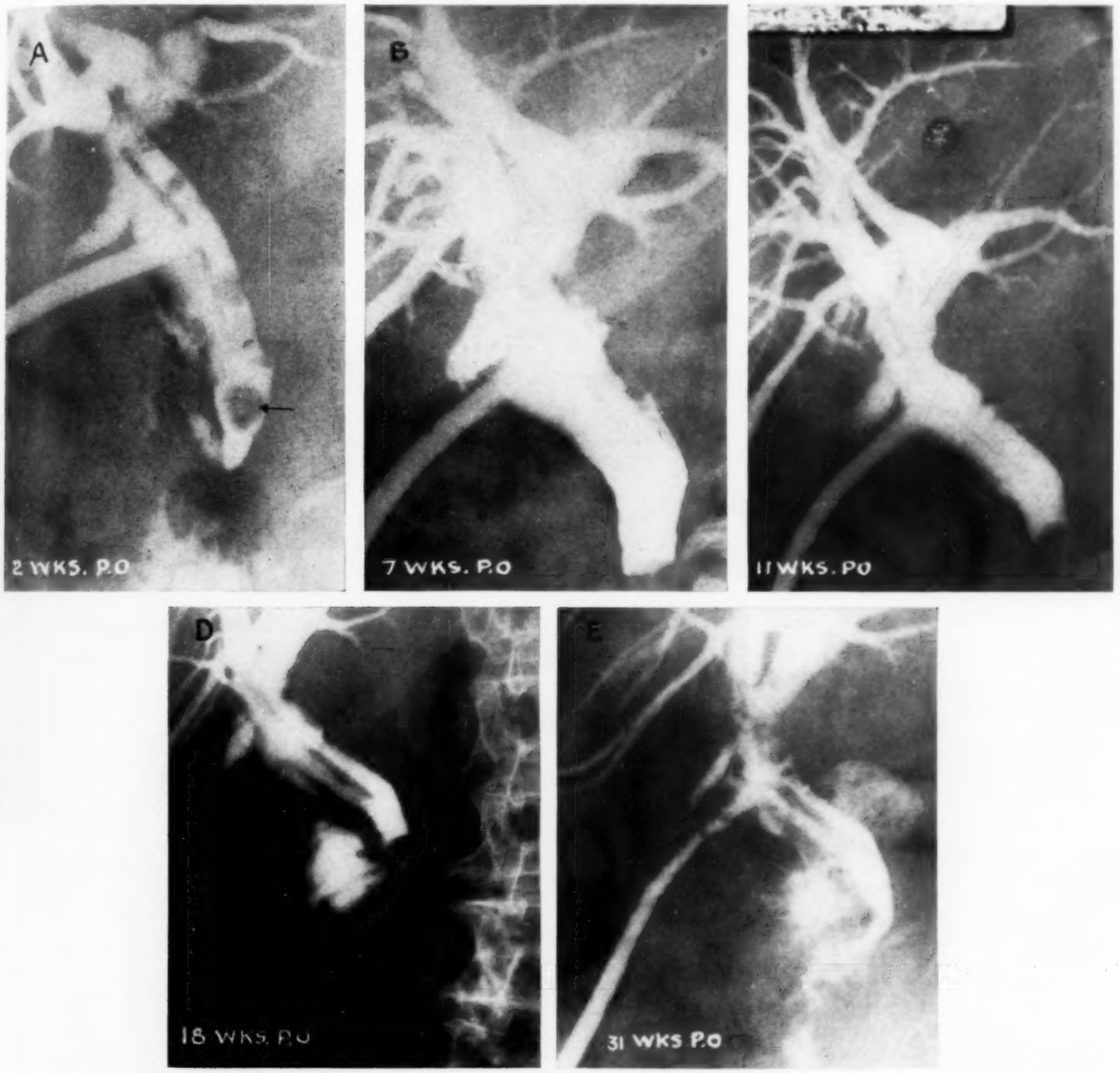


Fig. 2 (case 4).—Cholangiograms taken, *A*, 2; *B*, 7; *C*, 11; and, *D*, 18 weeks postoperatively, revealing "stone" in distal common duct with resultant partial obstruction and dilatation. *E*, normal cholangiogram, taken 31 weeks postoperatively.

The icterus index was 18 and the bilirubin level 2 mg. per 100 cc. On June 14, 1949, she had a cholecystectomy and common duct exploration. The gallbladder was inflamed and contained many stones. The common duct contained 50 to 75 stones varying from 2 to 5 mm. in diameter. There were also several stones in the right and left hepatic ducts. A lead probe passed readily into the duodenum. A cholangiogram performed Aug. 10, 1949 (seven weeks postoperatively), revealed several small filling defects in the terminal end of the common duct, although the iodopyracet passed readily into the duodenum. Another cholangiogram, taken Sept. 12, 1949, revealed slight narrowing at the distal end of the common duct and a probable partial obstruction; the filling defects were still present, but not so prominently as in the previous film. After June 25, the T-tube was clamped most of the time. However, there appeared to be definite obstruction, because by Sept. 30 the patient still had slight jaundice and complained of pruritus, along with alternating cholic and acholic stools. On Oct. 5 she was placed on therapy with 1 Gm. of bile salts four times a day. The cholangiogram taken Nov. 17, 1949 (21 weeks postoperatively), revealed a widened common duct, but the stone shadows were gone. The T-tube was removed early in December, 1949. When last seen, in August, 1955, the patient was well and had had no difficulty since the T-tube had been removed.

CASE 3.—A 52-year-old woman was admitted Dec. 20, 1951. Five weeks before admission she had developed sudden pain in the right upper quadrant radiating to the right subscapular area. Within a few days this pain was followed by jaundice, pruritus, acholic stools, and dark urine. The jaundice and acholic stools persisted up to time of admission and date of operation. The icterus index was 104, and the bilirubin content of the blood was 15.5 mg. per 100 cc. On Jan. 7, 1952, she had a cholecystectomy and common duct exploration. The common

duct appeared to be blocked about 1 cm. from the ampulla of Vater, but no stone was found through the opening in the common duct. Accordingly, we opened the duodenum to investigate the cause of the obstruction. The duodenal papilla was very small, and we were not sure that we actually identified it. We opened into the common duct at a point where the common duct lay immediately adjacent to the duodenal wall, as determined by proximity of the probe in the duct. We then probed the common duct upward from the papilla. However, we found an obstruction at a distance of 2 cm. that would not allow passage of a 6-mm. scoop. This stenosis was located in the head of the pancreas and may have been due to pancreatitis,

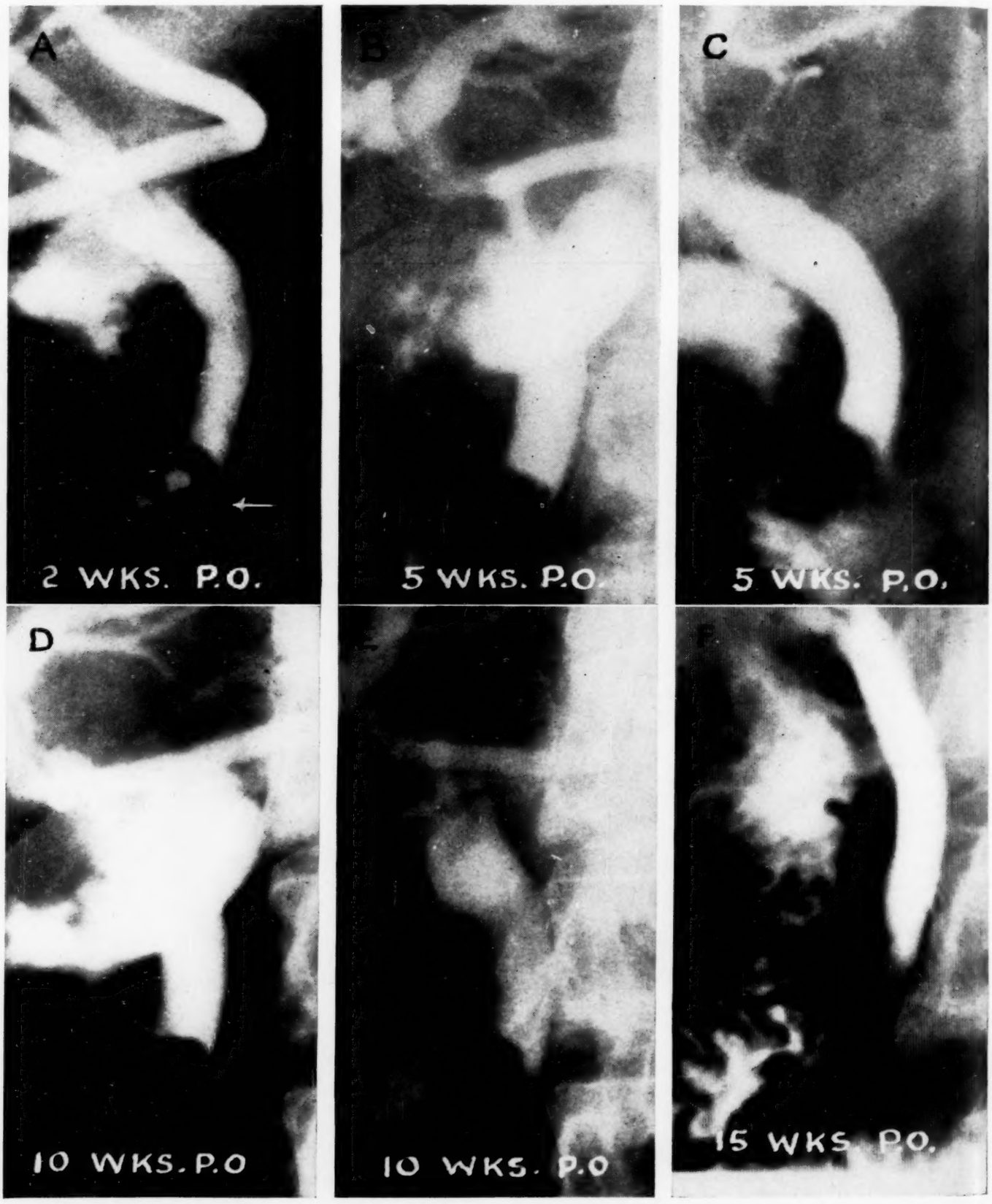


Fig. 3 (case 6).—Cholangiograms taken, *A*, 2; *B* and *C*, 5; and, *D* and *E*, 10 weeks postoperatively, revealing constant filling defect with incomplete obstruction. *F*, normal cholangiogram taken 15 weeks postoperatively.

although there was very little enlargement or induration of the head of the pancreas. In spite of prolonged manipulation, we were unable to find a stone that could explain the jaundice. On March 26, 1952 (11 weeks postoperatively), a cholangiogram was taken. A circular filling defect was noted in the distal end of the common duct, with a very small amount of opaque material passing into the duodenum around it. The film taken one hour later still showed marked retention of dye in the biliary tree, indicating that considerable obstruction existed. Another cholangiogram taken April 2 revealed a similar filling defect, and only a small amount of dye entered the duodenum. The patient was placed on therapy with 1 Gm. of bile salts four times a day, beginning April 2. A cholangiogram taken April 23, 1955, revealed absence of the "stone" shadow, and the iodopyracet flowed into the duodenum readily. It appeared that the major obstruction was now gone, but there was distinct narrowing of the common duct 2 cm. from the sphincter of Oddi. Although there no longer appeared to be obstruction of the common duct, we left the T-tube in place because of its narrowing. Cholangiograms taken May 7 and June 11, 1952, revealed no obstruction, but the narrowing was still present. Another cholangiogram, taken July 23, revealed the same findings. The T-tube was removed July 23. When last heard from, on Sept. 20, 1955, the patient said she had had no trouble since removal of the T-tube.

Case 4.—A 68-year-old man was admitted to the hospital on Oct. 28, 1954, with lower abdominal distress associated with constipation of two years' duration. About three weeks prior to admission he developed severe epigastric pain, with vomiting, chills, and a temperature of 104 F (40 C). The next day he noted that he had jaundice and that his urine was dark and his stools acholic. This attack gradually subsided, so that, at the time of admission, he had only slight jaundice. However, a few days after admission the pain, vomiting, and fever recurred along with deep jaundice. On Nov. 12, 1954, he had a cholecystectomy and common duct exploration. The gallbladder was small and shrunken. The common duct was dilated to a diameter of 4 cm. and contained two mulberry stones. The probe entered the duodenum with ease. A cholangiogram taken Nov. 26 (two weeks postoperatively) revealed a radiolucent shadow suggestive of a stone at the distal end of the common duct. The common duct was dilated proximal to this shadow (fig. 2). There was further evidence of obstruction in that, when the tube was clamped two weeks after operation, bile leaked around it to the exterior. The patient was placed on therapy with bile salts on Nov. 21, 1954. Cholangiograms performed on Jan. 5, Feb. 9, and March 30, 1955, revealed findings similar to those of Nov. 26. However, a cholangiogram performed June 15, 1955 (31 weeks postoperatively), revealed no evidence of stones; the common duct was of normal size and the iodopyracet entered the duodenum readily. The T-tube was removed June 15, 1955. When last seen, in September, 1955, the patient was asymptomatic.

Case 5.—A 59-year-old woman entered the hospital Dec. 29, 1952, complaining of flatulence, dyspepsia, and fatty-food intolerance of six months' duration. Ten days before admission she developed jaundice and had dark urine, although the stools were not acholic. The pain was variable. On Jan. 5, 1953, the patient had a cholecystectomy and common duct exploration. There were many stones in the gallbladder and common duct. Because the probe would not enter the duodenum, it was opened over the duodenal papilla. A sphincterotomy was performed, since the opening through the sphincter was no more than 1 or 2 mm. in diameter. A cholangiogram, done while the patient was on the operating table, was undiagnostic, since the ducts filled and the iodopyracet entered the duodenum. However, a cholangiogram done on Jan. 14, 1953 (two weeks postoperatively), revealed a constant filling defect that appeared to obstruct the flow of iodopyracet into the duodenum almost completely. Therapy with 1 Gm. of bile salts four times a day was started on Jan. 23, 1953. Cholangiograms performed Feb. 24 and March 11, 1953, were normal. The T-tube was removed March 11, 1953. When last heard from, on May 25, 1955, the patient was asymptomatic and had been so since the T-tube had been removed.

Case 6.—A 50-year-old man was admitted to the hospital in July, 1954, with a history of severe epigastric pain, chills, fever, and slight jaundice over a period of four or five days, two weeks before admission. The serum amylase level was elevated during this attack, being above 1,000 units per 100 cc. on one occasion. On his second admission, the patient was asymptomatic and no jaundice was present. At operation, stones were found in a badly diseased gallbladder. The head and most of the body of the pancreas were indurated and enlarged to at least two times the normal size. Stones and much bile precipitate were present in the common duct. The stones and precipitate were removed and a cholecystectomy performed; a T-tube was inserted in the common duct. Cholangiograms taken 2, 5, and 10 weeks after operation revealed constant filling defects (fig. 3). However, when the T-tube was clamped there was no pain or significant leak of bile. The patient was on bile salt therapy from the 2nd to the 15th week after operation. The cholangiogram taken 15 weeks after operation was normal, and the T-tube was removed. The patient has been completely asymptomatic up to the time of writing.

Case 7.—A 50-year-old woman was admitted to the hospital on Jan. 26, 1954. Three weeks previously she had developed severe right subcostal pain, followed in a few days by jaundice, acholic stools, and dark urine. On the patient's admission, the bilirubin content of the blood was 3 mg. per 100 cc. On Jan. 29, 1954, she had a cholecystectomy and common duct exploration. No stones were found in the common duct. A probe passed through the sphincter of Oddi, but with moderate difficulty. A cholangiogram taken Feb. 17, 1954, revealed a radiolucent defect in the common duct about 2 cm. distal to the exit of the T-tube. This was diagnosed as a stone. Treatment with 1 Gm. of bile salts four times a day was started at this time. Cholangiograms taken March 29, 1954, were normal, and the T-tube was removed. The patient has been asymptomatic since that date.

## Summary

During the past seven years we have encountered nine patients in the Illinois Research and Educational Hospitals who, after cholecystectomy and choledochostomy, had residual "stones" in the common duct as determined by cholangiography. All except one of these patients had been operated on in our hospital. All of these patients were treated conservatively for several months; treatment consisted of administration of 3 to 4 Gm. of bile salts per day by mouth in divided doses and continuous clamping of the T-tube. The "stone" shadows disappeared in seven of the nine patients in 8 to 31 weeks; in the two patients in whom the shadows persisted, operation was performed and the stones removed. In all patients the obstruction was incomplete, allowing clamping of the T-tube with flow of bile through the duct all the time. We would not expect this therapy to be successful if the T-tube could not be clamped, and would not try it. We have no proof that these shadows represented stones. All we can say is that they were suggestive of stones, and, on six or seven previous occasions when residual stones were diagnosed by cholangiography, we found stones at operation in every case.

840 S. Wood St. (12) (Dr. Cole).

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# PRESENT STATUS OF COBALT-60 TELETHERAPY IN THE MANAGEMENT OF THE CANCER PATIENT

Gilbert H. Fletcher, M.D., Houston, Texas

• *Cobalt-60 teletherapy is essentially a form of supervoltage radiation. There is no specificity of action on cancers by the various modalities of supervoltage, and it is a misconception to suppose that Co 60 teletherapy has something to offer when 2-million-volt x-ray therapy has not. Both offer the possibility of increasing the dosage of radiation to tumors because of better skin tolerance and a slight increase in tolerance of the deeper structures. But both must be used with due regard to the possible later appearance of subcutaneous and deep muscle fibrosis and other signs of cumulative damage, and the curability of a tumor is one of its fundamental biological properties. Supervoltage or Co 60 teletherapy is not indicated in a number of conditions, e. g., lymphomas in areas of superficial lymph nodes. Its use is elective in a number of other conditions, e. g., mediastinal and retroperitoneal lymphomas. Its use is imperative in a considerable number of conditions, including cancers of the oropharynx and urinary bladder and late cancers of the cervix and vagina. It has technical advantages that need to be explored further, but an objective and unemotional approach is necessary.*

The very rapid progress of atomic and nuclear physics in the last decade has resulted in new modalities of delivering radiation. High-energy generators, producing either x-rays or accelerated particles, and gamma ray–emitting isotopes, such as radioactive cobalt ($Co^{60}$) and cesium ($Cs^{137}$), have made possible a whole range of supervoltage (from 1 to 3 million volts) and megavoltage (above 10 million volts) equipment. It is unavoidable that misconceptions, unfounded hopes, and confusion will arise not only among physicians but in the public due to the extensive interest of the lay magazines in all matters pertaining to what is now called nuclear medicine. The specialist himself has difficulty in assessing the clinical value of these newly developed tools.

The increase of the number of deaths from cancer, due to the longer life span and the diminished incidence of deaths from other causes, is a factor in the greater awareness of cancer generally and motivates the intensified interest in all forms of cancer therapy. The physical and psychological trauma caused by the protracted length of the terminal stage in many cases of cancer produces conditions favorable for an emotional approach to any new development that arouses "last-straw hopes."

General practitioners, internists, and almost all the surgical specialists are connected with the management of cancer patients. On these physicians rests the responsibility of referring the patient to a skilled and properly equipped specialist or institution. Their role has a wide scope, as, in addition, they must advise the patients' families and be prepared to comment on the medical information that nowadays reaches the lay public. It is, therefore, essential that physicians have a background of factual knowledge about all the uses of radioactivity in the treatment of cancer, with special emphasis on their clinical usefulness or limitations.

$Co^{60}$ teletherapy is essentially a form of supervoltage radiation. The first million-volt machines were put into clinical use in the early 1930's. In other words, supervoltage radiation therapy is over 20 years old. The years preceding World War II saw further technological developments, but it was mostly during and after World War II that the tremendous expansion of atomic and nuclear physics brought about varied and powerful supervoltage and megavoltage devices, including the production, in the atomic reactors, of gamma ray–emitting isotopes with high specific activity, which can be used for external-beam therapy.

From the Department of Radiotherapy, University of Texas M.D. Anderson Hospital and Tumor Institute.

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Among those gamma ray–emitting isotopes, $Co^{60}$ is perhaps the most suitable for use in irradiators, which are, for all practical purposes, identical to 2-to-3-million-volt x-ray generators. The physical characteristics of the beam of a kilocurie teletherapy irradiator are essentially the same as those of the beam of the x-ray generators, and, therefore, the biological and clinical advantages in the treatment of human cancers are the same. The costs of production and maintenance of equipment may be less, but these factors have no bearing on the clinical effectiveness. This similarity of the beams is an important point, as it should dispel the rather widespread misconception that $Co^{60}$ teletherapy or $Cs^{137}$ teletherapy has any specific action in the treatment of human cancers.

$Co^{60}$ irradiators have been in clinical use for only four years, and most of the discussion that will follow is based on the longer experience with supervoltage radiation therapy. A review of the physical characteristics of supervoltage radiation and the fundamental principles underlying radiation therapy must be made prior to the discussion of the clinical advantages and indications in the various anatomic sites.

## Physical Characteristics of Supervoltage Radiation

The following physical characteristics of million-volt x-ray beams are pertinent to the treatment of human cancers: 1. The moist desquamation of the skin, which is inevitable at 200 kv., the level at which doses adequate for control of deeply located cancers are delivered, can be avoided. 2. The radiant energy

is not dispersed sideways outside of the beam, and, therefore, adjacent structures receive less radiation. In addition, the body as a whole absorbs less radiant energy, and, consequently, there is less systemic reaction, such as x-ray sickness, drop in blood cell count, or general fatigue. 3. A greater percentage of the energy reaches the deep-seated organs, and, therefore, it is possible to deliver larger doses to cancers in these organs. 4. There is less absorption by bone, which can be significant if there are bony structures between the surface of the body and the tumor to be treated, and, therefore, there is less risk of late osteonecrosis. All these characteristics are additive—to the effect that the physician can deliver greater tumor doses with less skin reaction, less systemic discomfort, and, up to a point, a better deep-organ tolerance.

Radiation of any kind (x-ray, gamma rays, and accelerated particles, such as electrons, protons, and alpha particles) always act through the same physical phenomena of ionization and excitation. These physical phenomena at the level of the atomic structure are responsible for the chemical changes that, in turn, are responsible for the biological changes that produce damage to all living cells. There is, at times, irreversible damage, making possible the sterilization of cancers. There are slight quantitative differences in the biological effectiveness of the different forms of radiation. Extensive physical and biological studies have demonstrated this difference to be from 10 to 15% more for the million-volt range than for the 200-kv. range. This difference is not specific for cancer cells but applies to all living cells. In practice, this means that, if, in order to sterilize a tumor, a tumor dose of 5,000 r in five weeks is necessary with 200-kv. radiation, 5,500-6,000 r is necessary with supervoltage radiation.

### Principles Underlying Radiation Therapy

Radiation therapy of human cancers is possible because some types of cancer have a greater sensitivity than the normal supporting structures. This margin of tolerance varies depending on the type of tumor and on the organ from which the tumor arises. This margin is usually very narrow. Tumor cells themselves are not affected differently by supervoltage radiation, but the deep-organ tolerance is somewhat increased, and, therefore, greater tumor doses are possible. For instance, in the treatment of tumors of the urinary bladder, 6,000 r in five weeks can be delivered to the whole bladder with supervoltage radiation without reactions unbearable to the patient, whereas 5,000 r cannot be delivered safely and without excessive discomfort to the patient in the same period of time using the 200-kv. equipment. Therefore, in this instance, there is a positive balance that is demonstrated by improved clinical results. The same holds true for irradiation of the whole pelvis in the late stages of cancer of the cervix and also for irradiation of the posterior third of the oral cavity and pharynx.

There is no specificity of action of supervoltage radiation on tumor cells as compared with radiation of 200 kv.; tumors that are normally radioresistant to medium voltage will stay resistant to supervoltage. For instance, melanomas, glioblastomata multiformeia, soft tissue sarcomas, and, by and large, the adenocarcinomas originating in the gastrointestinal tract are not benefited by supervoltage therapy. There are exceptions. For instance, the adenocarcinomas of the rectum that have some degree of radioresponse can at times be controlled with supervoltage radiation because much higher doses can be delivered. This can be put to advantage in inoperable tumors, or local recurrences. This form of therapy is not an alternate method for the classic abdominoperineal resection, which should be performed whenever possible. It is evident that the ability to deliver larger tumor doses is of most use in the treatment of those tumors that are moderately radiosensitive, such as the keratinizing epidermoid carcinomas and those that are located in areas inaccessible to the eminently effective interstitial or intracavitary radium therapy or in areas not directly available to low-voltage or medium-voltage radiation.

Larger volumes of tissue can tolerate only smaller doses of radiation. Recovery from the radiant energy comes from the surrounding undamaged structures, particularly blood vessels. The situation is very similar to the healing of wounds or burns, and recovery becomes slower and even impossible if large areas are overirradiated. Therefore, if the cancer is very extensive and the volume necessary to encompass the whole tumor is very large, the dose must be less if irreversible damage to vital structures is to be avoided. Unfortunately, the chance for permanent control decreases. At times, if a long-lasting control rather than a permanent cure is desirable, only part of the known tumor can be included in the beam in order to deliver sufficiently high doses. For instance, if the aim of treatment is to reopen the lumen in cancer of the esophagus and preserve this lumen until death occurs from distant metastases, one must limit the irradiation to the visibly obstructing part of the cancer.

The treatment of cancers with radiation is not different from the surgical approach. Instead of removing en bloc the volume of tissue that contains all tumor cells, one must deliver high doses of radiation to the same volume in order to sterilize all tumor cells. In the same way that surgery is limited by the problem of the removal of part or all of some vital structures, the necessarily high tumor doses are limited by irreversible damage incompatible with life.

When the cancer is too extensive or even more generalized, there is, of course, no form of radiation, irrespective of the modality and voltage, that can appreciably affect the course of the disease. However, radiation may be used for relief of one specific local symptom, oftentimes producing great benefit to the patient. The advantages of supervoltage radiation cannot be measured only by improved cure rates, with five-year survival being the criterion. The temporary control of distressing symptoms is very beneficial even if it does not prolong life. These clinical benefits can rarely be expressed in statistics.

In mentioning the advantages of supervoltage radiation, one tends to overlook the fact that its use is accompanied by limitations and late sequelae. It takes years for the subcutaneous and deep muscle fibrosis

to set in after heavy radiation treatment. The absence of acute skin reaction is very conducive to overenthusiasm and radical treatment. In addition, the skin-sparing effect tends to encourage the use of supervoltage radiation for the treatment of recurrences after previous radiation. This can be carried without any appreciable skin reaction, but unfortunately the previous damage to the inner structures, which never subsides, oftentimes causes exceedingly painful radionecrosis. It is only in rare circumstances, and with great conservatism, that re-treatments can be performed without excessive risks.

In many ways, the development of new radiotherapeutic tools and, in particular, supervoltage radiation can be compared with the advances in surgery and anesthesiology that have made possible more radical and, therefore, at times more effective procedures, resulting in appreciable clinical progress. They are not, however, a revolutionary approach. Greater skill and more clinical experience are necessary to adapt these powerful tools to the natural history of the disease processes with which one is trying to interfere. By and large, increased clinical benefits may be derived from supervoltage or $Co^{60}$ teletherapy in the area of those cancers that are neither radioresistant nor generalized when first seen and that, therefore, one can hope to control or cure.

*Usefulness of Cobalt-60 Teletherapy in Various Tumors*

| Not Indicated | Elective | Imperative | Special Studies Desirable |
|---|---|---|---|
| Head and neck | Esophagus | Extensive tumors of anterior ⅔ of oral cavity | Preoperative x-ray therapy for breast cancer |
| Skin and lip | Mediastinal and retroperitoneal lymphomas | All tumors of: Posterior ⅓ of oral cavity (fauces, tonsils, base of tongue, soft palate) | Some rectal cancers |
| Anterior ⅔ of oral cavity (early) | Seminomas | Paranasal sinuses | Some thyroid cancers |
| Vocal cords (early) | Occasionally bronchogenic carcinoma | Oropharynx and hypopharynx | Miscellaneous tumors |
| Nasopharynx with no involvement of base of skull | Ovarian cancers (localized to pelvis) | Extrinsic tumors of larynx | Locations where skin must be spared (metastases to pelvic bones) |
| Early cancers of cervix and vagina (intracavitary radium therapy) | | Inoperable neck nodes (postoperative recurrences) | |
| Postoperative breast irradiation | | Late cancers of cervix and vagina | |
| Lymphomas in areas of superficial lymph nodes | | Epidermoid carcinoma of: | |
| Bony metastasis | | Female urethra | |
| | | Urinary bladder | |
| | | Embryonal carcinoma of testis | |

In the epidermoid carcinomas accessible to low-voltage or medium-voltage therapy, such as cancers of the skin and lip, and in those epidermoid carcinomas optimally treated by interstitial or intracavitary radium therapy, such as the early cancers of the anterior two-thirds of the oral cavity or those of the uterine cervix, supervoltage therapy has nothing to offer and its use would even be a retrograde step. A review of the various anatomic sites and a discussion of the sites in which particular tumors can be handled best with supervoltage radiation (see table) are in order.

## Sites of Tumors and Radiation Therapy

*Head and Neck.*—Early epidermoid carcinoma of the anterior two-thirds of the oral cavity is still best handled by conventional means of interstitial radium therapy. In contradistinction, satisfactory results are not obtained in extensive tumors, and, if radical surgery is not indicated, supervoltage therapy offers a chance for more permanent cures or, at any rate, better growth restraint.

Even in the early epidermoid carcinoma of the posterior third of the oral cavity and oropharynx, results are unsatisfactory with conventional means of therapy. It is already a well-established clinical fact that supervoltage radiation offers a better chance for local control in this group of carcinomas. In addition to better control of the primary lesion, more adequate handling of the often-present metastatic nodes is possible with supervoltage therapy, especially in combination with radical neck dissection. In radical neck dissection after $Co^{60}$ teletherapy, there is not nearly as much danger of delayed wound healing.

With rare exceptions, the epidermoid carcinoma of the paranasal sinuses is rarely cured by radiation alone or by surgery alone. The combination of the two offers a better chance of control. Here too, postoperative radiation delivered with $Co^{60}$ can give a better distribution of the radiation and a higher tumor dose.

Supervoltage radiation also offers the possibility of control and possible cure in malignant tumors of the parotid gland—either primary adenocarcinoma, myoepithelial tumor, or metastases to the lymphatics of the parotid gland from epidermoid carcinoma. Here at times surgery followed by radiation is beneficial.

Inoperable metastatic nodes in the neck and postsurgical recurrences require high doses for control. If interstitial radium implant is not indicated, the $Co^{60}$ irradiator often produces sterilization of those masses.

The effectiveness and the place of radiation therapy in the management of thyroid cancer has never been definite. The advent of supervoltage radiation has not changed the basic policy of treatment, which should be primarily surgical. If, however, disease remains in a small area, let us say, on the trachea, high-dose radiation to a small volume can be delivered with the $Co^{60}$ irradiator and will possibly aid in control.

The early epidermoid carcinoma of the vocal cord can be handled very satisfactorily with 200 kv., although there is some advantage in using $Co^{60}$ because it produces less late skin change. In the treatment of the more extensive, extrinsic or intrinsic tumors of the larynx, if a laryngectomy cannot be performed or is refused, $Co^{60}$ teletherapy increases the possibility of cure over that with 200 kv. If radiation therapy fails, a laryngectomy can be performed with much less danger of delayed wound healing and necrosis.

*Thorax.*—The epidermoid carcinoma of the esophagus and the lung is incurable in the vast majority of cases because when it is first diagnosed the disease is too widespread. Two decades of radical surgical approach has taught us a great deal about the mode

of spread and causes of incurability. Oftentimes surgical resections or radiation treatment are utilized to relieve some specific distressing symptom.

The use of rotation technique at 200 kv. in the hands of Nielsen in Copenhagen has yielded very satisfactory palliation for cancers of the esophagus in some instances. In more than 80% of the cases so treated, the lumen was reopened and swallowing was possible until the time of death. Very little more can be expected with supervoltage radiation, and the only advantage of the use of a $Co^{60}$ irradiator is to simplify delivery of the radiation.

Whenever operable, bronchogenic carcinomas are best handled by surgery, as the unavoidable lung fibrosis, even with the use of supervoltage radiation, is a distressing symptom. It is only in the occasional early case of bronchogenic carcinoma that, due to the location, is unsuitable for surgery that radical radiation therapy is justified. In this instance, a simple arrangement of portals can be used with a $Co^{60}$ irradiator, but it must be remembered that, with skillful use of the multiple-portals technique, cures have been obtained in the past with 200 kv. No increase in cure rate can be expected from supervoltage radiation. Local control of mediastinal nodes producing obstruction of the superior vena cava can be achieved with tumor doses that can be delivered easily at 200 kv., although control can be obtained, perhaps with less systemic discomfort, by using $Co^{60}$ therapy. Actually grid therapy with 200 kv. is probably as good.

In those distressing instances of cancer of the thorax, any new therapeutic development always brings about almost mystical hopes. An extensive series of cases of both bronchogenic carcinoma and cancer of the esophagus has been treated with supervoltage therapy and always with very disappointing results. Supervoltage radiation offers little assistance in the management of these diseases.

*Female Genital Tract.*—Stage 1 and early stage 2 cancers of the uterine cervix are best handled by intracavitary radium therapy supplemented with moderate doses of external irradiation to the pelvic walls. Until physicians know more of the tolerance for external irradiation of the whole pelvis, the risks of late sequelae should be reserved for late stage 2, stage 3, and stage 4 cancers of the cervix, in which the cure rates are not satisfactory. High doses to the whole pelvis are possible with supervoltage therapy and are, therefore, worthwhile in the treatment of cancers that are spread throughout the pelvis. Preliminary impressions from several cancer centers seems to indicate that improved cure rates will result from supervoltage therapy in late uterine cancers. Advanced tumor of the vagina and all stages of epidermoid carcinoma of the female urethra are also best treated with supervoltage radiation.

Conventional techniques of intrauterine and intracavitary radium therapy followed by hysterectomy are still the best way to handle adenocarcinoma of the body of the uterus, and supervoltage radiation is only useful in those cases in which the tumor has spread beyond the confines of the body of the uterus.

In selected cases of ovarian tumor, in which surgery has left residual disease within the pelvis, the use of high tumor doses, possibly with supervoltage techniques, may add something to the management of the disease.

*Urinary Bladder.*—A tumor of the urinary bladder that is suitable for local treatment, such as electrocoagulation, local radiation, or partial cystectomy, of course, ought still to be handled by these methods. When total cystectomy has to be performed, supervoltage radiation should be considered, particularly if there are paravesticular masses. Although cure rates may not be greatly improved, one can produce growth arrest with much less discomfort and, therefore, can add to the patient's useful and comfortable life. Sufficient numbers of tumors of the urinary bladder have already been treated in various centers to demonstrate that supervoltage therapy is a definite addition in the management of those tumors.

*Tumors of the Testis and Lymphoma.*—Both the seminoma and lymphoma can be controlled by doses easily delivered with a 200-kv. generator. Supervoltage radiation makes the delivery of an adequate tumor dose easier for permanent sterilization of the retroperitoneal nodes or for long-lasting control of retroperitoneal or mediastinal manifestations of lymphoma. Embryonal carcinoma of the testis requires tumor doses that are difficult to give with medium voltage, and, although further study will have to be done, there is some possibility that somewhat improved cure rates can be obtained in these tumors by a better control of the retroperitoneal nodes.

*Miscellaneous Types.*—There are a number of tumors, usually rare, that show some varying degree of radioresponse, and, if they are located in such areas as the pelvis or the abdomen, the dosage necessary for cure or long-lasting control is more easily delivered with supervoltage radiation. For instance, a Ewing's sarcoma of the pelvic bones can be treated best with $Co^{60}$ therapy, because a higher tumor dose can be obtained with the necessary sparing of the skin.

At times, radiation for relief of pain due to bony metastases is better achieved with supervoltage radiation due to the utmost necessity of sparing the skin, for instance, the skin above the lower part of the back or the sacrum, so that the possibility of the development of decubitus ulcers when the patient becomes bed-ridden is diminished.

In selected cases, a resectable adenocarcinoma of the rectum with recurrences localized to the pelvis can be effectively controlled by supervoltage therapy.

The routine postoperative radiation of the internal chain of mammary lymph nodes and supraclavicular nodes after radical mastectomy is still probably best done with a 200-kv. generator. The depth dose of the supervoltage beam produces fibrosis of the lung and mediastinum that is not justifiable for this adjunctive therapy, which has never been uncontroversially proved to increase the survival rate in breast cancer. In the more advanced breast cancer in which surgery alone is no longer effective even in the control of the primary tumor and the regional lymphatics, a combination of preoperative radiation followed by mastectomy or of a simple mastectomy followed by heavy local radiation by the McWhirter method is indicated.

Radiation to the whole chest wall, in addition to the lymphatic areas, is imperative, and supervoltage helps diminish the severity of the skin reaction.

### Summary and Conclusions

The present status of cobalt-60 therapy or supervoltage radiation of the 2-million-volt range can be summarized by the following statements: 1. There is the possibility of increasing tumor doses because of better skin tolerance and a slight increase of the tolerance of the deeper structures. 2. There is no specificity of action on tumor cells and, therefore, no fundamental change in the radiosensitivity of tumor cells. 3. The modality of attack always has to be adapted to the natural history of the cancer, as its curability is fundamentally inherent in its biological behavior.

Supervoltage therapy is of no advantage in early accessible cancers treated optimally by low-voltage or medium-voltage x-rays (such as in cancer of the skin and lip) or by intracavitary or interstitial radium therapy (as in early epidermoid carcinoma of the oral cavity and uterine cervix). It does not offer assistance in radioresistant cancers and offers very little in the treatment of widespread cancers even if they are of the radioresponsive type. For instance, in bronchogenic carcinoma, supervoltage radiation offers very little more aid than does 200-kv. radiation and probably even no advantage over 200-kv. grid therapy for the relief of symptoms, such as mediastinal nodes pressing on the superior vena cava. In those cancers such as cancer of the esophagus no improvement in cure rates can be expected.

It is important to dispel some of the misconceptions concerning supervoltage therapy and $Co^{60}$ teletherapy. These misconceptions are responsible for grave disappointments as well as for the unfortunate physical and financial strain put on patients and their families by their seeking supervoltage therapy in faraway centers.

These misconceptions are (1) that supervoltage has anything to offer in generalized cancers, (2) that the radioresistant cancers are radiosensitive to supervoltage therapy, (3) that treatment of a recurrence after an original radiation treatment is feasible with supervoltage therapy, and (4) that there is any specificity of action on cancers by the various modalities of supervoltage, for instance, that $Co^{60}$ teletherapy has something to offer when 2-million-volt x-ray therapy has not.

It should be added that the newer forms of megavoltage equipment now in the process of clinical testing or development will also have no specificity of action. It is possible that, in some instances, there may be a further technical progress, but thorough clinical evaluation must be completed before any conclusions can be drawn. It is, however, doubtful that they will represent as great an improvement as the jump from 200 kv. to 2 million volts. Less skin reaction and less loss of radiant energy outside of the beam are the main advantages, and only some refinements will be obtained by further technological developments.

The task in the coming decade is more in clinical than physical treatment. Considerable experience is yet to be obtained in the adaptation of supervoltage therapy to those cancers that are still potentially curable in a certain percentage of cases but that have not been curable in the past due to the inability to control the primary disease and the proximal regional metastases. Also closer teamwork between the surgeon and the radiotherapist is in order, because supervoltage radiation broadens the possibility of combined surgery and radiation in many instances.

This clinical testing must be done with objectivity because overenthusiasm and misconceptions are too often conducive to rebounds to underrating the true possibilities. This happened in the 1930's after the first million-volt machines were built and put into clinical use. Primarily, the cases treated were hopeless, and, as results were very different from those achieved with conventional techniques, it was very hurriedly concluded that supervoltage radiation offered no advantage. It has taken over 15 years for the medical profession to recover from that premature misconception, and there is danger of the same thing recurring if an objective and unemotional approach to $Co^{60}$ teletherapy is not preserved.

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**Limitations of Chemotherapy in Tuberculosis.**—With the successful development of potent chemotherapeutic agents in the past several years the effectiveness of chemotherapy in human tuberculosis has not been limited by lack of effective antimicrobial drugs. This has been reflected in the high percentage of cures now possible in tuberculosis. It is perhaps no exaggeration to state that approximately 90 per cent of unselected and previously untreated cases now can be controlled with chemotherapy. This is true not only for pulmonary tuberculosis but similar results have been recorded in tuberculosis of bones and joints, tuberculous meningitis, genito-urinary tuberculosis, laryngeal tuberculosis, etc. . . . It is thus important from a practical clinical point of view to analyze the causes of chemotherapy failure. Moreover, such analysis leads to better utilization of chemotherapy and more effective application of accessory procedures such as surgery or collapse therapy. Sufficient experience has now accumulated to permit tentative efforts at such evaluation. These indicate that limitations of effective antituberculous chemotherapy at the present time stems from three sources: difficulties inherent in the nature of chemotherapeutic agents, those derived fromthe nature of the disease under treatment and, finally, those secondary to biological changes in the bacterial population itself.—I. J. Selikoff, M.D., The Chemotherapy of Tuberculosis, *Journal of the Mount Sinai Hospital*, July-August, 1956.

# BLOOD-GROUPING TESTS IN UNDISPUTED PATERNITY PROCEEDINGS

Leon N. Sussman, M.D.
and
Sidney B. Schatkin, LL.B., New York

• *Persons who were involved in litigation relating to paternity were invited to submit to blood-grouping tests after the cases had been settled by the defendant's admission of paternity. Cooperation was obtained in 67 cases, and the bloods were typed by the A-B-O system, the M-N system, and the Rh-Hr system. Three children were found by the A-B-O system not to be the offspring of the men who had admitted paternity; similarly the M-N and the Rh-Hr systems excluded three and two children respectively. In one of these instances a child was excluded by both the M-N and the Rh-Hr systems. It was probable that in 12 out of these 67 cases the men who had admitted paternity were not the actual fathers. Admissions of paternity were thus found unreliable. It is urged, in the interests of justice, that a blood test should be ordered in every case involving a charge of paternity.*

Heretofore use of blood-grouping tests, whose value has been firmly established by numerous investigators,[1] has been confined to those cases where the accused man has denied paternity. In these contested cases the scientific evidence of the infallibility of an exclusion based on blood tests is such that many states (New York, Maine, New Hampshire, New Jersey, Wisconsin, Ohio, Maryland, South Dakota, North Carolina, Pennsylvania, and Rhode Island[2]) have enacted statutes which make blood test exclusions decisive of the issue. However, the majority of men involved in paternity suits do not contest the charge. It is this group of cases with which this report is concerned.

In the courts where paternity cases are heard, only a minority of the accused men deny paternity. This group, therefore, are the only ones who are privileged to request blood tests to sustain their denial. It has been shown that 30 to 40% of these men who deny paternity are falsely accused.[3] In the majority of cases heard in these courts, however, the accused man admits paternity and accepts the burden of support imposed by the court.

Since no direct scientific findings can prove that the defendant is the father, the motivation for an admission of paternity is of interest. Usually it is one of these: (1) a sincere belief that he is the father, (2) a sense of pride arising from the fact that he could be the father, (3) a total lack of financial responsibility and, therefore, a careless attitude toward the situation, (4) inability to afford defense of the action and costs of blood tests and other evidence, or (5) a state of ignorance which confuses intercourse with paternity.

This report presents the findings in 67 cases of uncontested paternity where the involved persons submitted to examination after their suits were completed. All of these cases had been settled by the admission of paternity by the defendants, awards for support and expenses had been imposed, and the cases had been closed. Subsequent to all court actions, the involved parties then voluntarily submitted to blood-grouping tests. Obtaining the cooperation of these persons after their cases were completed was understandably difficult. The 67 cases represent the total number in which tests were completed in a three-year period during which over 500 litigants were interviewed and requested to submit to tests. The tests were performed in the usual manner of duplicate testing by different technicians using different lots of serum. ABO groupings were determined by direct cell typings with known anti-**A** and anti-**B** serum, and anti-A + **B** (O) serum, and by reverse typings with known A cells and B cells with the serum being tested. M-N groupings were determined with four anti-**M** and four anti-**N** rabbit serums by well and test-tube techniques. Rh-Hr groupings were determined by use of saline and "stick" tests with known **$Rh_0$, rh′, rh″, hr′,** and **hr″** antiserums in duplicate. Negative reactions were checked by use of antiglobulin techniques where pure or unblocked serum was used for the testing. ("Pure" or unblocked serum refers to a serum containing only a single antibody. Thus a pure **rh″** antiserum is obtained from a sensitized donor whose phenotype is $Rh_1rh$, thus lacking only the **rh″** factor. A blocked **$Rh_0$″** antiserum is not suitable for the antiglobulin test for this purpose, as the test would be falsely positive due to coating of the test cells by the univalent **$Rh_0$** antibody in the blocked serum.) Positive and negative controls were incorporated in each run. In addition to tests for accepted blood group systems listed in a report[4] on the "Medicolegal Application of Blood Grouping Tests," additional tests were done with anti-**Kell** serum and anti-**P** serum.

*Exclusions Obtained in Sixty-seven Cases of Uncontested Paternity*

| No. | Putative Father | Mother | Children | Excluded by System |
|---|---|---|---|---|
| 1 (Case 2) | O N $Rh_2rh$ | $A_2$ MN $Rh_2rh$ | $A_2$ M $Rh_1rh$ | M-N, Rh-Hr |
| 2 (Case 8) | O MN Rho | O M Rho | (a) O M Rho | Not excluded |
| | | | (b) $A_1$ M Rho | A-B-O |
| 3 (Case 16) | O MN Rho | B MN $Rh_1Rh_1$ | (a) O N $Rh_1Rh_1$ | Rh-Hr |
| | | | (b) O N $Rh_1rh$ | Not excluded |
| | | | (c) B MN $Rh_1rh$ | Not excluded |
| 4 (Case 21) | B M Rho | B M Rho | $A_1$ M rh | A-B-O |
| 5 (Case 39) | O M $Rh_2rh$ | O N Rho | (a) O N $Rh_2rh$ | M-N |
| | | | (b) O N $Rh_2rh$ | M-N |
| 6 (Case 56) | B N $Rh_2Rh_0$ | O M Rho | $A_1$ MN $Rh_1rh$ | A-B-O |

Attending Physician (Hematology) and Transfusionist, Beth Israel Hospital (Dr. Sussman) and Assistant Corporation Counsel of City of New York (Mr. Schatkin).

The results obtained, listed in the table, indicate that, of the 67 men involved in these cases of uncontested paternity action, 6 were absolutely excluded as the father of the involved child. As has previously been shown, blood groupings using the A-B-O, M-N, and Rh-Hr systems can exclude only 50% of the falsely accused men [1h]; it follows that, in fact, 12 or 18% of the accused men who admitted paternity were probably not the fathers of the children they accepted as their own!

## Comment

This report again emphasizes the need for use of all the available systems for blood grouping. Failure to test with antiserums to determine the subgroups of the Rh system reduces the value of the tests considerably. Thus, in this small series of six cases, involving seven children, three children were excluded by the A-B-O system, three by the M-N system, and two by the Rh-Hr system. One exclusion involved both the M-N and the Rh-Hr systems. Familiarity with these uncommon testing serums and a knowledge of the laws of genetics governing the inheritance of the blood factors are essential to the proper conduct and evaluation of the tests. For these reasons the medicolegal aspect of blood testing must be restricted to qualified experts.[5] The availability of rapid air transportation makes the expert laboratory easily accessible.

In this small series of "typical" cases of conceded paternity, 18% of the men are probably not the fathers of the children whose paternity they admit. This fact has a significant bearing on the reliability of admissions of paternity which are routinely and perfunctorily accepted daily in our courts. The courts should realize that 18% of the men who do not contest the charge are admitting paternity of children not their own. In the interests of justice, a blood test should be ordered in every case involving a charge of paternity.

## Summary and Conclusions

Blood-grouping tests in 67 cases of uncontested paternity indicate that in 6 cases, or 9%, the men admitting paternity were not the fathers of the children they accepted. Since only 50% of wrongfully accused men can be excluded by present methods of blood testing, it follows that not 6 but actually 12 men in this small series who admitted paternity were probably not the fathers of the children in question. The demonstrated unreliability of admissions of paternity should be drawn to the attention of the proper authorities.

36 E. 38th St. (16) (Dr. Sussman).

Technical assistance in this study was given by Mrs. Hannah Pretshold, M. S., M. T. (ASCP).

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**Nongonococcal Urethritis.**—The effectiveness of the intramuscular form of Terramycin as compared with some other standard forms of treatment in nonspecific urethritis was studied in 57 patients. Ninety-five per cent of the patients receiving either sulfadiazine or the oral form of Terramycin were considered cured or improved. Terramycin intramuscularly appears to be of some benefit in the treatment of nonspecific urethritis, although inferior to sulfadiazine and Terramycin orally. Of those patients receiving no specific therapy, about 65 per cent were considered cured or improved; this points up the difficulty in evaluating any new type of therapy. Bacteriologic studies and the nature of the responses to the various antibiotics used lead one to conclude that the hemolytic staphylococcus may play an important role in causing this disease. Nonspecific urethritis is a disease that may have a rather prolonged course and that is subject to spontaneous remissions and relapses. That it is acquired by sexual intercourse is surmised but by no means proved. Because of the apparent frequency of some degree of prostatic involvement "prostatourethritis" rather than "urethritis" would be a better term for the disease.—F. S. Wolf, M. J. Thoshinsky, Sanford Chodosh, and J. O. Arrington Jr., Therapy of Nongonococcal Urethritis, *United States Armed Forces Medical Journal*, June, 1956.

# INTESTINOVESICAL FISTULAS

## REPORT OF SEVEN CASES AND REVIEW OF THE LITERATURE

Benjamin S. Abeshouse, M.D., Martin A. Robbins, M.D., Mark Gann, M.D.
and
Julian O. Salik, M.D., Baltimore

• *Whether the cause of intestinovesical fistula is inflammatory, neoplastic, or traumatic, the mechanism of production is localized intestinal pathology, abscess formation, and extension to the bladder. The diagnosis is made from a history of passing gas and feces from the urinary tract. The best treatment is a multistage procedure, with the colostomy first, and then resection of the intestine and fistulous area of the bladder; cystostomy is not always necessary.*

Although relatively few articles have been written on the subject of intestinovesical fistula in the past 15 years, the literature prior to 1940 is replete with numerous reports. Our recent experience with the condition prompted this report of seven cases with a review of the literature and reevaluation of the subject from the standpoint of diagnosis and treatment.

Since ancient times, the passage of feces and air via the urethra has been considered pathognomonic of intestinovesical fistula. In 1888, Cripps wrote a classic study entitled "Passage of Air and Fæces from the Urethra."[1] Many of the fundamental facts and views elucidated by him are still valid today. He emphasized that in most cases, whether neoplastic or inflammatory in origin, secondary abscess formation rather than direct extension of the lesion was the chief factor in the production of fistulas. Those interested in the historical background of the subject are referred to the excellent review articles by Morrissey, Kellogg,[1A] Higgins,[2] and Parham and Hume.[3]

### Etiology

A simple classification of intestinovesical fistulas based on the etiology has been employed by many authors and divides these fistulas into five main types: (1) congenital, (2) traumatic, (3) inflammatory, (4) neoplastic, and (5) foreign body. A comparison of the relative frequency of the etiological factors is summarized in the table.

In recent years, there has been a noticeable change in the nature of the primary causative factors of this disease. This is borne out by the experiences at the Mayo Clinic. In 1921, Sutton,[4] of the Mayo Clinic, reported on 34 surgically treated cases, of which 38.23% were secondary to infection in the fallopian tubes and only 17.6% due to diverticulitis. Subsequently in 1950 Mayo and Blunt [5] collected 202 proved cases of diverticulitis seen at the Mayo Clinic between 1939 and 1948 and observed intestinovesical fistulas in 46, or 22.8%, of the patients.

There is little mention in the literature in regard to regional ileitis (Crohn's disease) as an etiological factor. Recently, Black and Bolt [6] and Williams [7] have reported single cases. Williams [7] collected 365 cases of regional ileitis, with 23 ileovesical fistulas. Robinson [8] reports three cases of ileitis with vesical fistula. According to Williams,[7] congenital fistulas are practically always associated with imperforate anus. Ladd and Gross reported 214 cases of imperforate anus and observed fistulas between the rectum and bladder in 117 of them.

Traumatic fistulas are produced either by external violence (chiefly gunshot wounds) or by surgical injury. The latter type may occur after instrumentation, i. e., passage of a metallic sound, cystoscope, or resectoscope, or during surgery. Williams [7] noted 22 traumatic cases in a series of 148 intestinovesical fistulas. Ten of the 22 cases occurred after prostatectomy; most of them were rectourethral or at the bladder neck. In all probability, traumatic fistula is more commonly encountered than reports would indicate. We have seen three cases of intestinovesical fistula resulting from operative trauma, i. e., after suprapubic prostatectomy, resection of posterior bladder for neoplasm, and operation for imperforate anus. These cases have not been included in this report.

Inflammatory conditions represent the most common cause of fistulas. Not infrequently the primary causative lesion in cases of inflammatory fistula is an unsuspected carcinoma of the intestine or other adjacent organs whose presence is revealed at operation or autopsy. In the majority of instances of intestinovesical fistula, regardless of the cause, there is abscess formation and extension to and communication with the bladder. The chief primary inflammatory disease encountered is diverticulitis of the sigmoid. Regional enteritis is next in frequency. Rarely, fistulas may form as a result of appendicitis or cecal or pelvic inflammatory disease.

Neoplastic disease ranks a close second to inflammatory disease as a causative agent. Carcinoma of the rectosigmoid is the most common lesion. In the series of 34 cases collected by Higgins [2] at the Cleveland Clinic, 13 were due to carcinoma of the lower part of the intestine, i. e., 7 sigmoid, 2 rectosigmoid, and 4 rectal. Neoplasms of the bladder or female pelvic organs are rarely primary causative factors.

There have been scattered reports of the production of intestinovesical fistulas as a result of ingestion of foreign bodies. Herbst and Miller [9] reviewed the literature and reported a case that occurred after the patient had swallowed a chicken bone. The chief offenders have been bones and pins swallowed acci-

From the departments of urology (Drs. Abeshouse and Robbins), surgery (Dr. Gann), and radiology (Dr. Salik), Sinai Hospital.

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dentally. In a few instances, there was some doubt as to whether the foreign body was ingested or inserted via the urethra. In most cases the foreign body becomes lodged in the lower part of the intestine and initiates an inflammation with perforation, abscess formation, and fistula.

Appendicovesical fistula represents a rare type of fistula. Pemberton and co-workers [10] reported only five cases from the Mayo Clinic. In three of these cases there was an antecedent history of acute appendicitis. Goldstein [11] reported a case in which a biopsy was performed and fulguration done on a tumor on the right lateral wall of the bladder. The tumor subsequently proved to be the appendix protruding into the bladder.

It is of interest to note that intestinovesical fistula occurs more frequently in males than females (3:2). The interposition of the uterus between the intestine and the bladder apparently serves as a defensive barrier against the spread of infection from the sigmoid colon to the bladder in the female.

*Relative Incidence of Different Types of Intestinovesical Fistulas as Found by Various Authors*

| Author | Intestinovesical Fistula | | | |
|---|---|---|---|---|
| | Congenital | Traumatic | Neoplastic | Inflammatory |
| Higgins[2] | 21 | 60 | 113 | 168 |
| Kellogg[1a] | 3 | 20 | 16 | 51 |
| Ewell and Jackson: J. Urol. 46:693, 1941. | ... | 1 | 7 | 3 |
| Sutton[4] | ... | 3 | 2 | 29 |
| Ormond and others: Surg. Gynec. & Obst. 89:411, 1949 | ... | 3 | 14 | 8 |
| Williams[7] | 6 | 22 | 64 | 51 |
| Total | 30(5%) | 109(15%) | 216(33%) | 310(47%) |

## Pathogenesis and Symptoms

The mechanism of production of an intestinovesical fistula is essentially the same whether the cause is inflammatory, neoplastic, or traumatic. The primary requisite is localized intestinal pathology with perforation, abscess formation, and extension to the bladder. The lower part of the intestine, with its many virulent organisms, is often the chief site because of its proximity to the bladder. The two most common conditions in the rectosigmoid, i. e., diverticulitis and carcinoma, are the frequent causative agents.

There are two pathways by which the infection spreads to the bladder: 1. Adherence to the bladder via an abscess. In this manner, as in diverticulitis, a marked peridiverticulitis develops with abscess formation and adherence to the bladder and subsequent rupture into the bladder. This mechanism is commonly described in the literature. 2. Extension of an inflammatory or suppurative process from the diverticulum along the mesosigmoid and/or the ureter to the base of the bladder and thence into the bladder. This mechanism was encountered in four of our seven cases of fistula. We have found only scant reference to this in the literature. Since the most common site of intestinovesical fistula is in the region of the trigone of the bladder and ureteral orifice, which are retroperitoneal structures, it is our belief that the latter is a more common pathway of spread than has been appreciated up to this time.

In most instances, it is difficult, in either the fresh or the fixed specimens, to identify the fistulous tract. Usually, the tract is so tortuous that it defies dissection, and one sees only a mass of chronic inflammatory tissue. Mayfield and Waugh [12] made a careful pathological examination of specimens in 32 cases of sigmoidovesical fistulas, and in only one case was the fistulous tract definable.

In the fully developed case of intestinovesical fistula, the diagnosis can be made from the history. The usual story is one of passing gas and feces via the urinary tract, with concomittant urgency, frequency, and dysuria due to the associated cystitis. There may be hematuria in the later stages. Symptoms and signs of the primary causative disease may also be present. In most cases, there is pain in the lower part of the abdomen and constipation. The fistulas in the lower part of the colon usually do not lead to passage of urine into the colon. The higher the site of the intestinal communication, the more likely it is for urine to appear in the stool. In ileovesical fistulas, the patient will frequently pass urine per rectum.

Many authors have emphasized a stage in the development of the disease prior to the actual fistula formation. In this prodromal stage, in which there is abscess formation and pericystitis, the only symptoms indicating the disease may be those referrable to the bladder. Lazarus and Marks [13] emphasized an incipient stage before fistula formation, when the threatened breakthrough is manifested by the sudden onset of frequency, urgency, burning, pyuria, and albuminuria. When the breakthrough occurs, it may be explosive in onset, with severe tenesmus and strangury due to the acute cystitis. This may then pass into a chronic stage. Some patients may have pneumaturia and fecaluria for several years before they seek help. Mayo and Blunt [5] noted an average duration of symptoms of 18.5 months in 48 patients with vesicosigmoid fistula before they sought medical care.

The diagnosis is suggested by the clinical history and physical signs. Cystoscopy may be of value in establishing the diagnosis. During the incipient stage, one may observe a localized area of cystitis with edema and engorgement of the vessels, generally on the left side near the base of the bladder. After fistula formation, there is edema, marked cystitis, and particulate fecal matter in the urine. One rarely observes the actual fistulous opening because of the associated inflammatory changes and bullous edema.

Proctosigmoidoscopy has virtually little diagnostic value. The fistula may be demonstrated by either a cystogram or a barium enema. When in doubt, one may instill methylene blue or sodium indigotindisulfonate (indigo carmine) in the bladder and recover it in the stool. One may also feed the patient charcoal by mouth and recover the substance in the urine.

## Treatment

No single mode of treatment is applicable to all cases. The method depends upon such things as the general condition of the patient, the nature of the disease in the intestine, the status of the urinary tract, and the duration of the condition. In general, it is agreed that a multistaged procedure is best.

Mayo and Blunt [5] recommended preliminary colostomy in cases of vesicosigmoidal fistula. In two patients in whom the fistula was divided and the opening in the sigmoid and bladder closed, there was a recurrence of previous signs and symptoms. In 46 patients treated by a preliminary colostomy the mortality was lowest (6.5%). Balch reported 19 cases of vesicosigmoidal fistula and noted that the patients in whom attempts were made to close the fistula before colostomy was performed did poorly. Rankin and Brown [14] stated that "any attempts to locally excise the fistula without bowel resection is doomed to failure" and stressed the value of preliminary colostomy. This stand is also advocated by Kellogg [1A] and by Sutton.[4]

It is now the accepted practice to perform the colostomy first and then resect the intestine and fistulous area of the bladder. It is not always necessary to perform a cystostomy. The bladder can be closed primarily and drained per urethra.

The length of time elapsing between colostomy and resection depends upon the general improvement of the patient. Occasionally, the fistula may close spontaneously after the fecal stream is diverted, but this does not preclude further section. In the poor-risk patient or in the patient with inoperable carcinoma a permanent colostomy may be adequate palliation. In one of our reported cases (case 5), the elderly patient refused further surgery after the colostomy and was content to live in that manner.

Mayo and Miller [15] reviewed 88 cases of sigmoidovesical fistula treated surgically at the Mayo Clinic and reported that 35 patients were cured, 5 improved, 4 unimproved, and 4 had recurrence. There were 26 deaths related to the primary disease or operation. The above statistics substantiate the fact that this condition is a serious disease and requires diligent and long-term care.

## Report of Cases

Case 1.—A 55-year-old woman was admitted to the hospital on March 31, 1949, with a complaint of chills and fever and nausea and vomiting for the previous three months. In addition, there was marked shortness of breath and orthopnea. The patient was treated at home with penicillin, but the fever recurred. The patient also complained of low back pain and pain in the bladder region after voiding. She stated that she had seen gas bubbles in her urine since October, 1948. She had a history of rheumatic heart disease with congenital septal defect.

Physical examination revealed an acutely ill, malnourished female. The temperature was 103 F (39.4 C). The blood pressure was 115/70 mm. Hg. The patient was dyspneic and orthopneic. There were rales at both bases and a systolic murmur in the pulmonic area. Abdominal examination revealed a tender mass in the suprapubic area. On pelvic examination there was a rectovaginal fistula. There was also generalized immobility of the pelvic structures suggesting a pelvic abscess or neoplasm. There were gas bubbles in the catheterized bladder urine. The urine appeared grossly cloudy and had a fecal odor. Microscopic examination revealed numerous pus cells, and there was 1+ albumin. The urine culture revealed Escherichia coli and Proteus vulgaris. A barium enema revealed diverticulosis and diverticulitis of the sigmoid colon. Cystoscopy was not performed. She was placed on a regimen of streptomycin and daily creosol douches. A preoperative diagnosis of diverticulitis of the sigmoid with abscess formation was made.

On April 7, 1949, a pelvic puncture was attempted through Douglas' pouch and the anterior bladder wall, but the mass was noted to be firm. On April 11, 1949, an exploratory laparotomy was performed, and a large mass involving the sigmoid and bladder was noted in the pelvis. A transverse colostomy was performed. The patient was discharged on April 24, 1949.

She was readmitted on June 5, 1949, and on June 9, 1949, a rectosigmoid resection and telescoping anatomosis were performed. Pathological examination revealed diverticulitis with peridiverticulitis and abscess formation involving the bladder. Postoperatively, she was placed on therapy with bishydroxycoumarin (Dicumarol). She developed a purulent drainage from the lower angle of the wound, and a large abscess was opened. Methylene blue was put into the distal loop of the colostomy and came through the drainage area. The drainage gradually diminished. On July 5, 1949, the colostomy was closed. On July 8, 1949, the patient died suddenly, and the presumptive diagnosis was pulmonary embolus. An autopsy was not performed.

Case 2.—A 59-year-old man was admitted to the hospital on Oct. 31, 1947, with the complaint of hematuria. The patient had noted bloody urine for the first time two weeks prior to admission. One year before that, a bladder tumor (papilloma) had been resected transurethrally at another hospital. He stated that he had had frequency, urgency, and nocturia for five years.

Fig. 1 (case 2).—Cystogram showing dye (3.5% sodium iodide) passing from bladder into rectosigmoid.

The history and system review were essentially negative except for chronic constipation for the past 12 years, for which he had taken laxatives regularly.

Physical examination revealed a well-developed, well-nourished, elderly male, not acutely ill. The temperature was 99.8 F (37.7 C), and the blood pressure was 108/80 mm. Hg. Heart and lungs were normal. The bladder was distended to the umbilicus. Examination of the genitals revealed a dark bloody discharge from the penis. At the base of the penis was a red, tender area. The presumptive diagnosis was (1) recurrent bladder tumor; (2) abscess of the penis; (3) benign prostatic hypertrophy, grade 1; and (4) right inguinal hernia. The urine contained 15 white blood cells per high-power field.

On admission to the hospital, the patient was catheterized, and two emesis basins full of bloody urine with new and old clots were obtained. Cystoscopy was performed shortly afterward, and a small vesical calculus with diffuse cystitis was noted. Retrograde pyelography disclosed normal kidneys. The abscess in the penis was incised and drained. Thereafter, the patient continued to show pus in the urine. Urine culture

revealed Esch. coli. The patient also ran a spiking fever, and on the third day after cystoscopy he began to drain fecal matter per catheter. A cystogram was performed, and the dye passed from the bladder into the sigmoid (fig. 1). Cystoscopy was repeated, and the findings were unchanged. No definite fistulous opening was seen. Findings from a gastrointestinal series and a barium enema were negative.

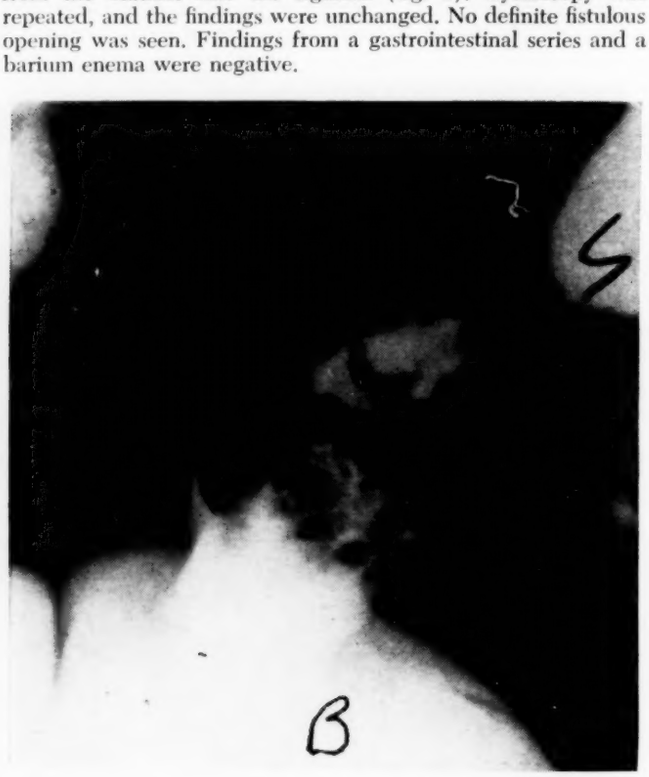


Fig. 2 (case 3).—Barium enema showing fistulous tract (F) extending from sigmoid (S) down to bladder (B).

The patient was prepared for operation by the use of a Miller-Abbott tube and the administration of phthalylsulfathiazole (Sulfathalidine). At operation, the sigmoid was found adherent to the bladder and markedly inflamed. The involved portion of the sigmoid and bladder were removed in toto, and end-to-end anastomosis was performed on the sigmoid. A suprapubic cystostomy was also performed. The pathology report indicated a diverticulitis of the colon with perforation, abscess formation, and vesicosigmoid fistula. The patient made an uneventful recovery and was discharged as cured.

Case 3.—A 52-year-old woman was first admitted to the hospital on Oct. 23, 1950, with the complaint of pain in the left lower quadrant of the abdomen of two weeks' duration. She had also noticed pain in the left costovertebral angle with radiation into the left groin. At times the pain was quite sharp and colicky in nature. During this time, the patient had occasional nausea and vomiting. There was no change in bowel habits. She also had epigastric pain and anorexia. There was weakness and generalized malaise. She had had vaginal bleeding on two occasions in the past five years. A gynecologic operation, whose exact nature could not be determined, had been performed two years before at another hospital. She had had an appendectomy 30 years before. The patient had noticed moderate frequency of urination, slight burning on urination, and nocturia (she urinated three or four times nightly) for several years.

Physical examination disclosed the patient to be well developed, well nourished, and chronically ill. The heart and lungs were normal. Blood pressure was 96/70 mm. Hg. Examination of the abdomen revealed tenderness in the left costovertebral angle and along the left side of the abdomen. There was also tenderness in the midline above the symphysis. There was also an irregular mass palpable in the left lower quadrant. Urinalysis was negative. The serum urea level was 31 mg. per 100 cc. The hematocrit reading was 41%. The white blood cell count was 9,750 per cubic millimeter, with a normal differential count. Cystoscopy revealed a filling defect caused by pressure on the posterior wall of the bladder from without. There was no evidence of ulceration or fistula formation in the bladder. The findings on bilateral retrograde pyelograms were negative. A barium enema revealed diverticulitis and inflammatory abscess extending into the bladder with possible intrinsic polyps in the rectum (fig. 2).

An exploratory laparotomy was performed, and a mass the size of an orange was found lying on the anterior surface of the uterus. The mass involved the sigmoid and bladder and left adnexa, and a presumptive diagnosis of diverticulitis with abscess formation and incipient intestinovesical fistula was made. A colostomy was performed. The patient made an uneventful recovery.

She was readmitted on Dec. 31, 1950, and a resection of the sigmoid colon and left adnexa was performed. The mass was freed from the bladder by blunt and sharp dissection and did not perforate through the wall of the bladder. Examination of the excised specimen revealed marked diverticulitis and peridiverticulitis with abscess formation of the sigmoid colon. The patient made an uneventful recovery. She was readmitted on Feb. 8, 1951; at that time closure of the colostomy was performed. The patient was discharged as cured.

Case 4.—A 49-year-old man was admitted to the hospital on June 5, 1953, with the chief complaint of pain in the lower part of the abdomen. Four days prior to admission the patient had noted the sudden onset of pain in the left lower quadrant of the abdomen with a feeling of pressure over the bladder and urgent desire to urinate. There was no incontinence, hematuria, or pyuria. The pain continued until the day prior to admission. At that time the pain in the left lower quadrant of the abdomen became quite severe and colicky and was accompanied by nausea and vomiting. There was no diarrhea or blood in the stool.

Physical examination revealed a well-developed, well-nourished, middle-aged male who appeared to be very uncomfortable because of pain in the abdomen. The blood pressure was 142/90 mm. Hg; the pulse rate was 100 and the respiration rate 16 per minute. Examination of the abdomen revealed tenderness

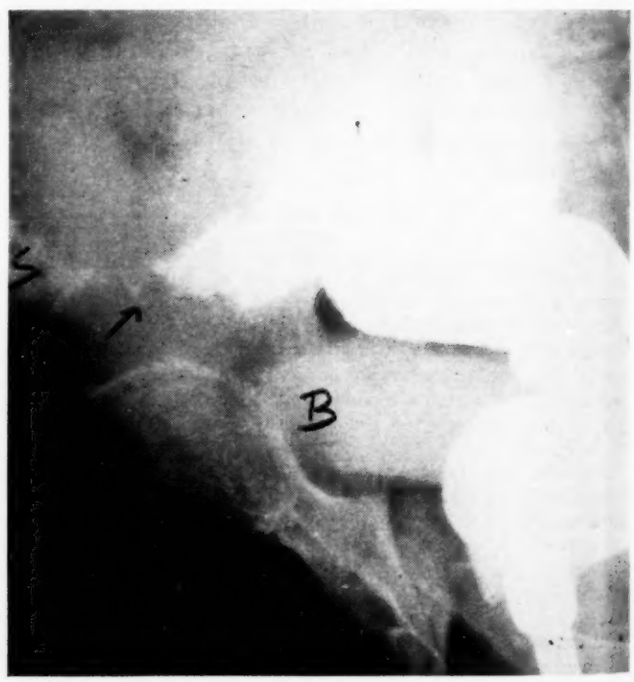


Fig. 3 (case 4).—Barium enema (lateral oblique film) showing fistulous tract (F) between sigmoid (S) and bladder (B).

in the left lower quadrant with rebound. There was no mass palpable. Rectal examination was negative. The genitals were normal. The bladder did not appear to be distended. Cystoscopy was not performed, but cystography revealed a filling defect on the superior aspect of the bladder with displacement of the entire bladder to the left. Excretory urography was negative. The urine showed 5 to 10 white blood cells per high-power

field, with 1+ albumin. A barium enema was performed and revealed diverticulitis and diverticulosis of the sigmoid colon with a fistulous tract extending into the bladder (fig. 3).

On June 8, 1953, an exploratory laparotomy was performed, and in the midportion of the sigmoid there was an abscess surrounding an area of presumed ruptured diverticulum extending down toward the bladder and firmly adherent to the bladder. There was marked induration of the mesentery. A transverse colostomy was performed. On June 10, 1953, the patient passed gas through the urethra. Methylene blue was instilled in the distal loop of the colostomy and appeared in the urine. This established diagnosis of intestinovesical fistula. The postoperative course was stormy, with high fever. The patient was given chlortetracycline (Aureomycin) hydrochloride and neomycin sulfate, and his fever subsided. He was discharged on June 25, 1953.

On Sept. 23, 1953, the patient was readmitted for operation, which disclosed that the sigmoid colon was involved in an inflammatory mass. The sigmoid was resected and an end-to-end anastomosis performed. The patient made an uneventful recovery and was discharged on Oct. 1, 1953. He was readmitted to the hospital on Dec. 27, 1953, for closure of the colostomy. This was done without incident, and the patient was discharged on Jan. 6, 1954, as cured.

Case 5.—A 70-year-old man was admitted to the hospital on Aug. 3, 1953, with the chief complaint of anorexia, lethargy, and weight loss for the past five months. He had also noted intermittent diarrhea, which at times became debilitating. For several days prior to hospital admission, he had had severe pain in the left lower quadrant and progressive difficulty in voiding. His stools had been very watery for a few days prior to admission. There were no bloody or tarry stools. No hematuria was observed. Language difficulty made it almost impossible to obtain an accurate history from this patient.

Physical examination revealed him to be an elderly male who appeared acutely ill, dehydrated, and in a toxic condition. The blood pressure was 80/60 mm. Hg; the temperature was 101.2 F (38.4 C); and the pulse rate was 96. Examination of

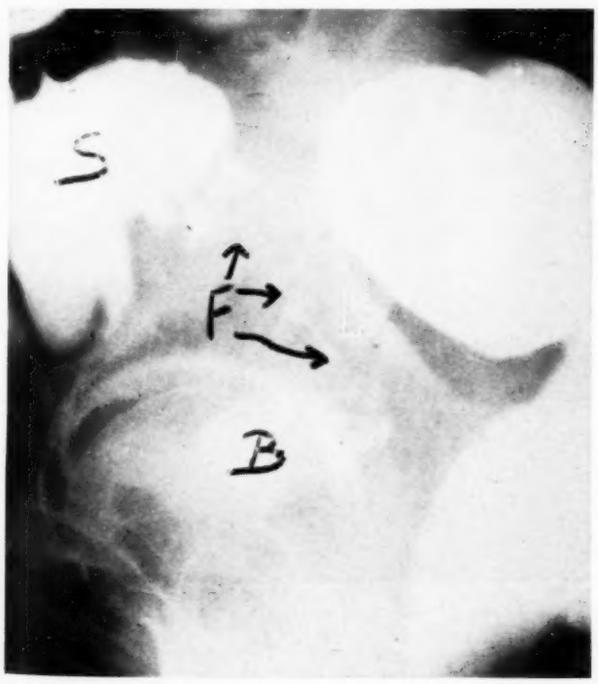


Fig. 4 (case 5).—Barium enema (lateral oblique film) showing fistulous tract (F) between sigmoid (S) and bladder (B).

the abdomen revealed marked distention with rebound tenderness in the left lower quadrant. There was no mass. Borborygmi were heard. The genitals were normal. Rectal examination revealed a 2+ benign enlargement of the prostate. On the anterior wall of the rectum there was a firm, irregular shelf-like mass, which was not tender. The patient was catheterized, and an indwelling Foley catheter was inserted. About 300 cc. of foul-smelling urine, with a fecal odor, was obtained. Proctoscopic examination to a distance of 17 cm. was negative for pathology. The barium enema was performed, and on fluoroscopic and radiographic examination it was disclosed that there was a narrowing in the region of the sigmoid. The barium seemed to escape through a fistulous tract into the bladder (fig. 4). Several diverticula were present in the sigmoid.

Fig. 5 (case 6).—Barium enema (lateral oblique film) showing fistulous tract (F) between sigmoid (S) and bladder (B).

Excretory urography was performed and revealed prompt bilateral excretion, but the outline of the upper urinary tracts was poor in detail. Urinalysis revealed urine with a fecal odor with 4+ albumin. The urine contained innumerable red blood cells, white blood cells, and casts. Culture of the urine revealed Esch. coli.

On Aug. 6, 1953, operation disclosed a firm, lemon-sized mass in the region of the sigmoid above the peritoneal reflection. There was free fluid in the abdomen. The large intestine proximal to the lesion was dilated, edematous, and reddened. There was a firm mass adherent to the posterior wall of the bladder. A transverse colostomy was performed. The patient had a prolonged convalescence with fever and protracted anemia. He developed a leukopenia and neutropenia and was given multiple blood transfusions. Uremia and pneumonitis ensued but cleared with intensive treatment.

On Aug. 21, 1953, cystoscopy was performed, and enlarged prostatic lateral lobes were observed. There was bullous edema and tumefaction in the right midline on the posterior lateral wall. On Sept. 4, 1953, the barium enema was repeated, and the retrograde flow of barium failed to show the fistula. On Sept. 21, 1953, cystoscopy was repeated and essentially the same findings noted. On Sept. 23, 1953, excretory urography was performed and the left genitourinary tract failed to visualize. On Oct. 14, 1953, a barium enema was performed that showed diverticulitis and diverticulosis of the sigmoid and a perforated diverticulum producing a fistulous tract leading to the bladder. The patient's condition improved, and further surgery was advised but refused. He was discharged with the colostomy functioning. He failed to return for further observation.

Case 6.—A 51-year-old man was first admitted to the hospital on April 27, 1954, with the complaint of having passed dark brown urine for three months. The urine had an odor of stool. One month prior to admission, he had begun to notice that he had frequency and nocturia and intermittent low back pain. The review of the other systems was negative.

Physical examination revealed a well-developed, well-nourished, middle-aged male, not acutely ill. The blood pressure was 130/80 mm. Hg. There was a questionable mass in the left lower quadrant in the region of the large intestine, which was tender. The genital organs were normal. Rectal examination was essentially negative. Excretory urography revealed normal pelves, calyces, and ureters on both sides. There was a pressure

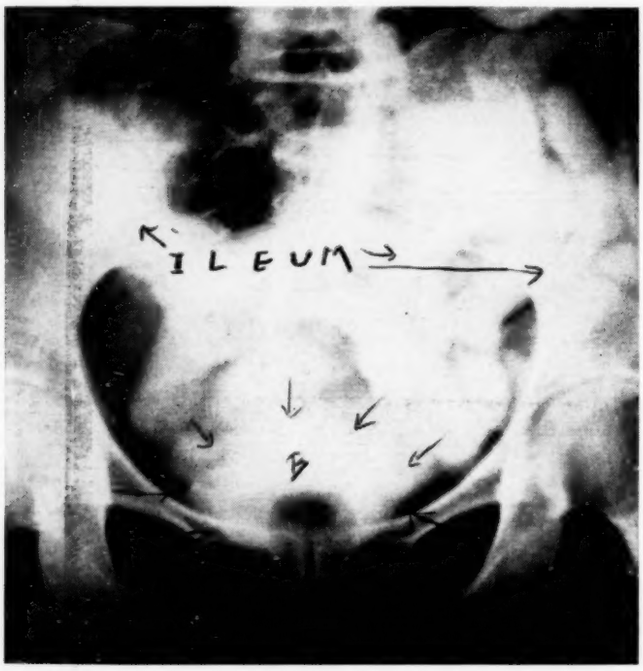


Fig. 6 (case 7).—Cystogram showing dye (3.5% sodium iodide) passing from bladder (B) into ileum (I).

defect on the fundus of the bladder that appeared to be due to an extrinsic mass. On April 28, 1954, cystoscopy revealed the bladder to be inflamed, and on the left side there was a mass extending from the vesical neck onto the posterior wall with marked bullous edema. No definite fistulous tract could be seen. A barium enema was performed and revealed a fistulous tract between the terminal ileum and the sigmoid and between the sigmoid and bladder (fig. 5) and diverticulitis of the sigmoid and distal third of the descending colon.

On May 11, 1954, a transverse colostomy was performed, and during operation a large inflammatory mass was found incorporating the sigmoid, colon, bladder, and small intestine. On Aug. 11, 1955, the patient was readmitted to the hospital. At operation, the sigmoid was removed after the small intestine was freed up and a sigmoidosigmoidostomy and a suprapubic cystostomy were performed. The small intestine and omentum were markedly adherent to the mass. When the sigmoid colon was opened in the excised specimen, a probe could be passed through a fistulous tract into a portion of the excised bladder. The patient had an uneventful postoperative course. On Sept. 27, 1955, the patient was readmitted to the hospital for closure of the colostomy and had an uneventful course thereafter.

Case 7.—A 54-year-old woman was first admitted to the hospital on Feb. 3, 1955. She gave a history of having had a carcinoma of the cervix for which she had received radium therapy and deep x-ray therapy in 1938. She had developed a stricture of the right ureter and had been receiving periodic ureteral dilatations. In 1953, there was no evidence of recurrence of the carcinoma. On Sept. 1, 1954, a right nephroureterectomy was performed for a massive hydropyoureter and for hydronephrosis. At that time the patient had suffered from recurrent chills and fever.

The patient stated that she had been passing urine per rectum for three weeks prior to her last hospital admission. She had also passed scant amounts of urine through the urethra with great difficulty. She had not urinated through the urethra for several days prior to her hospital admission.

Physical examination revealed a fairly well-developed, well-nourished female, not acutely ill. The blood pressure was 170/90 mm. Hg; the pulse rate was 108; the temperature was 98.6 F (37 C). Examination of the abdomen revealed generalized tenderness with no masses. The blood urea level was 104 mg. per 100 cc. The hematocrit reading was 35%. The urine showed many red blood cells and a few white blood cells, with clumps and 2+ albumin. Cystoscopy was unsatisfactory because of marked inflammation. Excretory urography revealed the left ureter to be dilated. Cystography revealed a communication between the bladder and ileum (vesicoileal fistula) (fig. 6). Findings from the barium enema were negative. A cystogram revealed the bladder to be trabeculated, and the dye passed readily into the ileum. A small intestinal series showed the barium passing from the small intestine into the bladder (fig. 7) and remaining there for more than six hours. An electrocardiogram was compatible with coronary insufficiency. Proctosigmoidoscopy was negative.

On Feb. 11, 1955, an exploratory laparotomy was performed and revealed the ileum to be adherent to the bladder. The intestine was resected, exteriorized, and drained, and the small intestine was reunited end to end. The patient was discharged on Feb. 26, 1955. She was readmitted on March 15, 1955, with the complaint of generalized abdominal pain and the passing of stool in the urine. A cystogram revealed a sigmoidovesical fistula at this point. Excretory urography showed a marked hydronephrosis on the left with a hydroureter. Abdominal operation was performed, and the intestine and a portion of the bladder to which it was attached were excised. A transverse colostomy and a ureterocutaneous anastomosis on the left were performed.

The patient had a very stormy postoperative course and went rapidly downhill. She died with fever and septicemia on April 27, 1955. Autopsy revealed recurrent carcinoma of the

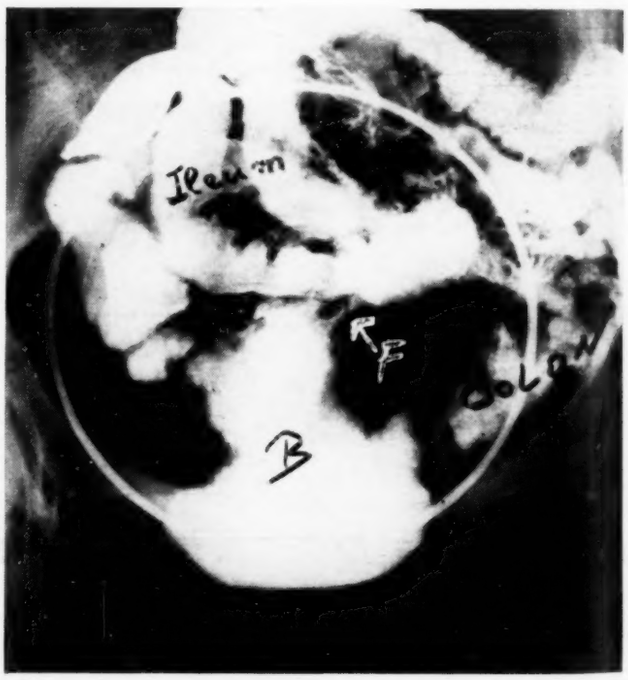


Fig. 7 (case 7).—Barium enema showing fistulous tract (F) between ileum and bladder (B).

cervix with extension into the uterus and bladder and a vesicosigmoid fistula. There was metastasis to the liver, mesenteric lymph nodes, and intestinal tract. There was generalized pelvic peritonitis.

## Summary and Conclusions

Five of seven patients with intestinovesical fistula were in the sixth decade of life; the youngest was 49 years of age and the oldest 70 years. Four were males and three females. The etiological condition responsi-

ble for the intestinovesical fistula was, in six cases, diverticulitis with abscess formation extending downward and into the bladder; in the remaining case, the fistula was secondary to a carcinoma of the cervix. A solitary fistula was present between the sigmoid and the bladder in the five cases due to diverticulitis and accompanying abscess formation. In four of these cases the abscess opening was located in the posterior wall of the bladder in or adjacent to the trigone. In one case (case 3), true fistula formation was not demonstrated in the bladder, as the abscess from the diverticulitis extended down to but not through the bladder wall; thus the diagnosis is a presumptive one and the condition may be regarded as being diagnosed in the prefistulous or incipient stage. One patient (case 6) also had a fistula between the sigmoid and ileum.

A correct preoperative diagnosis was established in five cases (cases 1, 2, 5, 6, and 7), in each of which fecal particles were seen in the urine. The fistulous communication between the bladder and sigmoid was demonstrated by cystography, i. e., passage of dye from the bladder into the intestine in two cases (cases 2 and 7) and by passage of barium from the intestine into the bladder in four cases (cases 3, 4, 5, and 6).

Operative treatment was carried out in each case with only two mortalities: the patient in case 1 died of pulmonary embolus on the third postoperative day after closure of colostomy, and the one in case 7 died of septicemia after a lengthy operation consisting of a combined excision of the vesicosigmoidal fistulous tract, transverse colostomy, and a ureterocutaneous anastomosis on the left. One patient (age 70) obtained a good result after a transverse colostomy and refused further surgery. In other cases, with the exception of case 2, multistaged operative treatment was employed consisting of (1) colostomy, (2) excision of fistulous tract and resection of intestine, and (3) closure of colostomy. In case 2, a one-stage operation consisting of excision of fistulous tract, end-to-end anastomosis of intestine, and suprapubic cystostomy was successfully performed. A suprapubic cystostomy was employed in only one other case (case 6).

A review of the literature and personal experience with seven cases warrant the following conclusions. Intestinovesical fistula is a serious condition presenting difficult problems in diagnosis and requiring a carefully planned multistaged operative treatment. The condition can be classified according to the most common etiological factors, in order of frequency, as follows: (1) inflammatory, (2) neoplastic, (3) traumatic, (4) congenital, and (5) foreign body. In the majority of cases of intestinovesical fistula there is an associated abscess formation with extension to and communication with the bladder. The diagnosis of intestinovesical fistula is suggested by the clinical history, that is, passage of gas and feces in the urine with concomitant urgency, frequency, and dysuria, and the physical signs, that is, pain, tenderness, and a mass in the left lower quadrant.

Cystoscopy may be of value in establishing the diagnosis. In the fully developed case, edema, marked cystitis, and particulate fecal matter in the urine are usually observed but the fistulous opening is not visualized due to the bullous edema and inflammatory changes. In the incipient stage, localized inflammation and edematous changes and inward bulging of the posterior bladder wall at or near the trigonal area are noted. The fistulous opening may be demonstrated not infrequently by either a cystogram or barium enema. Occasionally, instillation of methylene blue or sodium indigotindisulfonate (indigo carmine) into the bladder may lead to recovery of the dye in the stool. Surgical treatment varies with the duration and severity of the pathological process. In most instances the best results have been obtained by employing a multistaged operative plan, namely, (1) colostomy, (2) combined excision of fistulous tract and intestinal resection, and (3) closure of colostomy.

The early diagnosis of diverticulitis with or without abscess formation and the institution of prompt surgical treatment will prevent the development of intestinovesical fistula. Close cooperation between the gastrointestinal specialist or internist, the surgeon, the urologist, and the radiologist will insure early diagnosis and appropriate surgical treatment.

100 W. Monument St. (1) (Dr. Abeshouse).

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# BETA-PROPIOLACTONE IN STERILIZATION OF VACCINES, TISSUE GRAFTS, AND PLASMA

Frank W. Hartman, M.D.
and
Gerald A. LoGrippo, M.D., Detroit

• *Beta-propiolactone seems to be a superior sterilizing agent for biologicals because of its capacity to inactivate a wide variety of bacteria, fungi, and viruses. At the same time, this chemical has a minimal effect on proteins, avoiding final neutralization, and produces relatively nontoxic end products. The rapid penetration of tissues allows safer and more homogenous tissue grafts of arteries, bone, and cartilage. Although use of the product against the hepatitis viruses has not been studied, since this is yet not possible, beta-propiolactone produces plasma that will keep for long periods and will be well tolerated by patients.*

The usual process of sterilization by physical or chemical methods results in radical changes in the medium or environment containing the micro-organism concerned. The sterilization of biologicals, such as vaccines, tissue grafts, and plasma, involves as the first consideration, beyond that of the lethal effect on the micro-organisms, the preservation of the proteins in or near their original state. In the case of vaccines, preservation of the bacterial or virus proteins in their original state should be attained as far as possible so that the resulting antigen will produce antibodies comparable to those obtained using the same organisms in the viable state. In the case of plasma, denaturization of the proteins is to be avoided so that they will remain nontoxic and nonantigenic and will retain their normal in vivo functions and survival. In the case of tissue grafts, it is essential to obtain nontoxic, nonantigenic material that will function without producing complications when transferred to the patient.

The efficiency of heat, the most efficient and widely used physical bactericidal agent, is paralleled by the coagulation of proteins. The same is true of the two bactericidal chemical agents, phenol and formalin, which are most commonly used in biological applications. These chemical agents have the further disadvantage of remaining intact in the end-product and, hence, may be toxic when used in plasma, tissue grafts, or vaccines.

It is well established that a number of virus infections in man are accompanied by a phase of viremia. Some of these, such as serum and infectious hepatitis, produce a carrier state resulting in clinical cases of hepatitis in the recipient of such a carrier's blood. With the constantly increasing utilization of blood, blood plasma, homologous tissue grafts, and vaccines, it becomes imperative to develop methods of sterilization that will insure the maximum safety and effectiveness of these various products.

Over the last five years more than 500 chemical compounds have been screened,[1] with special emphasis on the finding of one that would inactivate the virus of serum hepatitis in blood and blood plasma. Beta-propiolactone appears superior to other chemicals tried, and satisfactory methods of processing the biologicals have been developed and applied in a relatively large group of patients.

## Properties of Beta-propiolactone

Beta-propiolactone was first synthesized by Johannson[2] in 1915, who used the silver salt of beta-iodopropionic acid, but Beckurts and Otto attempted to make it in 1885. Kung, in 1941, found a method of synthesizing beta-propiolactone from ketene and formalin and assigned the patent to the B. F. Goodrich Company. Since that time the substance has been studied and produced by Gresham and co-workers[3] in the research center of the Goodrich company. In 1950, beta-propiolactone was furnished to us by Parke-Davis & Company for evaluation in our screening.[4] All the beta-propiolactone was obtained subsequently through the courtesy of Gresham and the Goodrich company.

This chemical is a colorless, stable liquid in its concentrated form, but it is quite unstable in aqueous solutions. It is best kept at –20 to –30 C in plastic or neutraglass sealed containers. It has a specific gravity of 1.149 and is 37.5% soluble in water at 25 C. It reacts readily with hydroxyl, amino, carboxyl, sulfhydryl, and phenolic groups.

Beta-propiolactone has been reported[5] as a more effective sterilizing agent for a wide variety of viruses, bacteria, and fungi, including their spores (table 1). Our studies show that sterilization can be attained with concentrations of the chemical that do not denature the plasma and tissue proteins to any objectionable extent. This method has already been successfully employed clinically for the sterilization of plasma, sterilization of tissue grafts, and the preparation of virus vaccines.

## Sterilization of Plasma

Previous publications give, in more detail, the advantages of beta-propiolactone over mechlorethamine hydrochloride (nitrogen mustard), dichlorodiemethylsulfide (mustard gas), ethylene oxide, the photodynamic action of dyes, or ultraviolet irradiation for the inactivation of numerous viruses artificially seeded in plasma and those naturally occurring in plasma during the stage of viremia.[1] Extensive studies from this laboratory also show that a wide margin of safety exists between the virucidal and the toxic concentrations of beta-propiolactone. Since the hepatitis viruses have not been successfully studied in the experimental laboratory, the ultimate effectiveness of beta-propiolactone

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against these agents remains in question. Although plasma treated with a 0.6% solution of beta-propiolactone is nontoxic to man upon intravenous administration, this concentration is one and one-half times that necessary to inactivate the most resistant laboratory virus (that of eastern equine encephalomyelitis) and 12 times that necessary to inactivate the most sensitive virus (that of lymphocytic choriomeningitis) when these agents are seeded in plasma. However, in order to maintain the integrity of the plasma proteins, a 0.45% concentration of beta-propiolactone should not be exceeded. Since a concentration of 0.3% of beta-propiolactone in transfusion units of icterogenic plasma is not sufficient to inactivate the last-trace quantities of hepatitis virus present, the combination of beta-propiolactone and ultraviolet irradiation previously reported[6] has been extensively studied and the technique for use on large volumes elaborated.

Animal experiments with the eastern equine encephalomyelitis virus clearly show that there is always an additive and often a synergistic virucidal effect with beta-propiolactone and ultraviolet irradiation.[7]

The maximum degree of virus inactivation can be obtained by the use of a combination of from one-third to one-fourth of the beta-propiolactone concentration and from one-third to one-fourth of the ultraviolet irradiation as when either agent is used alone. What is more important is the fact that the combination can be used in marked excess of that necessary for sterilization and the integrity of the plasma proteins, as demonstrated by electrophoresis, will still be maintained.[7b] With a wider range between the dosage necessary for sterilization and that bringing about protein alteration, the combination shown here is the most promising available method for inactivating the hepatitis virus in human plasma.

Plasma treated with 0.35% solution of beta-propiolactone plus ultraviolet irradiation in the intensity recommended by the National Institutes of Health standards, produces a product that is clear amber in color, keeps for long periods, and is well tolerated by patients. Over 100 units of treated plasma has been administered to infants and adults without any untoward, immediate or delayed, reactions.

TABLE 1.—*Beta-propiolactone Concentration Required for in Vitro Sterilization of Micropathogens*

| Pathogens | No. of Pathogens Tested | Sterilizing Concentration of Beta-propiolactone, Gm./100 Cc.* |
|---|---|---|
| Viruses | 8 | 0.05 to 0.30 |
| Bacteria | | |
| Vegetative forms | 7 | 0.1 to 0.20 |
| Spore forms | 2 | 0.5 to 0.75 |
| Fungi | 5 | 0.25 to 0.50 |

* Viruses require a lower concentration for sterilization than either bacteria or fungi. Spore forms require the highest concentration of beta-propiolactone for sterilization.

## Sterilization of Grafts—Arteries, Bones, and Cartilage

The problems confronting surgeons who are interested in a tissue bank are, first, how to obtain sufficient arteries, bone, and cartilage to meet the demand of today's advanced techniques in surgery and, second, when such tissues are available, how to be certain that these are free from infectious micro-organisms. Arteries can only be obtained from dead persons by special grants from relatives. Bone and cartilage can be obtained from the living in limited quantities, whereas an adequate supply can be obtained from dead persons if there is efficient sterilization.

The actual use of tissue grafts sterilized by beta-propiolactone is based on extensive animal experiments.[8] Arteries and bones were placed in heavily seeded material, incubated for two hours at 37 C, treated, and then transferred to suitable mediums and/or animals to enhance the growth of any micro-organisms that might survive the sterilization.

TABLE 2.—*Depth of Tissue Sterilization with One Per Cent Solution of Beta-propiolactone After Bacteremia and Viremia in Susceptible Hosts*

| Conditions | | Results—Sterilization of Tissue Thickness, Mm. | | | | Controls | |
|---|---|---|---|---|---|---|---|
| Pathogen | Susceptible Host | Artery | Bone | Kidney | Liver | Bacterial Count* | Virus Titer† |
| Escherichia coli | Rabbit | 3 | 6 | 3 | 3 | $8\times10^8$ | ... |
| Pneumococcus (type 3) | Mouse | 3 | ... | 3 | 3 | $9\times10^5$ | ... |
| MM strain, encephalomyocarditis virus | Mouse | 3 | 3 | 3 | 3 | ... | 3.6 |
| Lymphocytic choriomeningitis virus | Guinea pig | 3 | 3 | 3 | 3 | ... | 3.9 |
| Eastern equine encephalomyelitis virus | Rabbit | 3 | 3 | 3 | 3 | ... | 4.4 |

* Count per gram of tissue in kidney tissue.
† Virus titer $LD_{50}$ is the reciprocal of negative logarithm (base 10) of virus dilution. Tissue sterilization can be accomplished at a depth of 3 mm. or less for compact tissue and up to 6 mm. for cancellous bone. In virus studies, thickness of bone did not exceed 3 mm.

In a second group of experiments, tissue slices were obtained from infected animals during the stage of bacteremia or viremia.[9] These specimens included arteries, bone, kidney, and liver, ranging from 1 to 9 mm. in thickness, which were treated with 1% solution of beta-propiolactone (table 2). The bone samples were sawed from ribs, giving an outer, thin, compact layer and the cancellous inner portion.

Tissue treated with 1% solution of beta-propiolactone appears well preserved upon microscopic examination. However, its failure to grow in tissue culture shows it is not viable. It has been found that certain tissues need not be viable to function temporarily. The nonviable tissues that have proved acceptable are arteries, bone, and cartilage, providing they are nonantigenic and sterile.

From October, 1954, to March, 1956, arteries sterilized with beta-propiolactone have been used at the Henry Ford Hospital in 120 operations with good results.[10] This use was preceded by two years of experimental work in dogs.[8] Since July, 1955, bone and cartilage have been used in over 30 operations with equal success.

## Antigenicity of Beta-propiolactone-Inactivated Virus Vaccines

In the preparation of inactivated virus vaccines, the margin between complete inactivation and the amount of antigenicity retained is so narrow that the search for more satisfactory methods has been intense. In a previous report[11] and in studies in progress, beta-propiolactone appears to have advantages over other chemicals for the preparation of inactivated virus vaccines.

It inactivates viruses completely and irreversibly in from 10 to 15 minutes at 37 C, whereas inactivation with formalin and phenol requires several days under the same conditions. Beta-propiolactone can be added in excess of the minimal, effective, virucidal concentration with a margin of safety between the complete inactivation of viruses and loss of antigenicity. Moreover, significantly higher degrees of antigenicity have been obtained with beta-propiolactone-inactivated virus vaccines than with phenol-inactivated or formalin-inactivated vaccines under parallel conditions.

Formalin-inactivated and phenol-inactivated viruses of murine encephalomyocarditis, eastern equine encephalomyelitis, and rabies were compared with the same viruses inactivated with beta-propiolactone. Formaldehyde (0.12% solution) inactivated the MM virus in 24 hours, while beta-propiolactone (0.2% solution) inactivated the same virus in 10 minutes. No antigenicity titer could be demonstrated for the formalin-treated MM material, while material treated with a 0.2% solution of beta-propiolactone gave a titer of $10^{-2.5}$. Phenolized rabies virus gave a resistance index of less than 10 as compared with a resistance index of 125 in material treated with a 0.2% solution of beta-propiolactone. Treatment with beta-propiolactone also gave an antigenic response with MM virus almost as high as with the live virus. These results have been confirmed by other investigators.[12]

## Summary

Beta-propiolactone is a superior sterilizing agent for biologicals because of its rapid and irreversible action, minimal alteration of proteins, and complete hydrolysis, obviating neutralization and toxicity. Preservation of proteins and relatively nontoxic end-products of hydrocrylic and beta-chloropropionic acids makes beta-propiolactone the most promising chemical for the sterilization of blood plasma. Rapid killing of bacteria and inactivation of viruses with maintenance of comparatively high antigenicity offers a method for the production of improved vaccines. Activity on a wide variety of bacteria, fungi, and viruses, coupled with rapid penetration of tissues, opens the way for safer and more plentiful homogeneous tissue grafts of arteries, bone, and cartilage.

2799 W. Grand Blvd. (2) (Dr. Hartman).

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**Hypertension.**—Effective treatment of hypertensive emergencies requires an agent which will reduce the blood pressure quickly and effectively. It is fortunate that a choice of drugs is available at this time. However, the potency of many of these agents is such that an intimate knowledge of pharmacodynamics of them is necessary if they are to be employed with maximum efficiency and safety. The very potency of many of these agents makes them dangerous if improperly employed. Marked elevation in blood pressure itself, even though due to many different causes, may become a direct threat to the patient's life if not brought under immediate control. This is so even though the elevated blood pressure may be only a part of the clinical syndrome. Under these circumstances control of the blood pressure can become the primary therapeutic problem and, in fact, can become a life saving procedure. The more important disease entities in which hypertension can become an emergency are acute nephritis, toxemia of pregnancy, hypertensive encephalopathy, pheochromocytoma, fulminating heart failure due to essential hypertension, hypertensive crisis, cerebral hemorrhage with severe hypertension, renal artery occlusion and others.—J. H. Moyer, M.D., and E. W. Dennis, M.D., Treatment of Hypertension, *Southern Medical Journal*, June, 1956.

# INDUCED HYPOADRENALISM IN PATIENTS REQUIRING ORTHOPEDIC SURGERY

James A. Nicholas, M.D., Philip D. Wilson, M.D.
and
Charles J. Umberger, Ph.D., New York

*• Prolonged administration of steroids often, but not always, results in adrenocortical insufficiency. It has been difficult to determine whether a patient so treated is actually devoid of adrenocortical function. Elective surgery on bones and joints in such a patient should be postponed until his adrenal status is ascertained and he has been weaned away, if necessary, from the steroid. The test used for this purpose consists in administering corticotropin and determining daily salt excretion during a period of constant salt intake; hypoadrenalism is likely to exist if the corticotropin fails to reduce the salt excretion and especially if it fails to induce eosinopenia and hypokalemia. Ten patients who had been receiving steroids (for seven years, in one instance) underwent orthopedic surgery. The above test was carried out in nine and revealed adrenal insufficiency in six. The diagnosis was borne out by the occurrence of shock in four of the patients and the effectiveness of hydrocortisone given intravenously in combating it. In cases of elective surgery the operation can be postponed for several months to permit weaning, but, when emergency surgery is required in a patient who has been receiving cortisone, increased amounts of steroid will be needed during and after the operation.*

Hypoadrenocorticism is increasing in frequency because of the increased variety and use of steroids in the treatment of a number of diseases. This has produced a growing problem for those of us who are called on to operate on such patients for injury or reconstruction of their bones and joints.[1] Orthopedic surgeons in particular should be cognizant of the symptoms and management of sudden adrenocortical insufficiency during and after surgery or injury, since a number of patients who receive cortisone acetate or other steroids come under their treatment for reconstruction.

Hypoadrenocorticism may result from several conditions. It may be induced by the administration of steroids. It results from adrenalectomy or hypophysectomy, procedures in vogue today for treatment of certain cancers, from hyperplasias of the pituitary adrenal system, and from hypertension. It occurs in adrenal cortical hypofunction (Addison's disease). Finally, it may occur as a result of adrenal tuberculosis, amyloid disease, and other pathological conditions of the adrenals.

## Effect of Long-term Use of Steroids

There are many corticosteroids on the market today. Among them are cortisone, hydrocortisone, fludrohydrocortisone acetate, prednisone (Meticorten), prednisolone (Sterane), Co-Deltra (buffered prednisone), and Co-Hydeltra (buffered prednisolone). Other preparations, which include salicylates (such as Sigmagen [tablets containing prednisone, aspirin, ascorbic acid, and aluminum hydroxide] and Salcort [tablets containing cortisone acetate, sodium salicylate, dried aluminum hydroxide gel, calcium ascorbate, and calcium carbonate]), are also being widely used. Some confusion has been produced among doctors and patients alike by the variety of trade names for the identical steroid. The fewer side-effects these steroids have, the more widely they are used. However, one side-effect that has not been diminished is induced hypoadrenalism, which may result from therapy with steroids over a long period of time. That these steroids are potential adrenal suppressors, causing functional and pathological adrenal atrophy, has been well established by Bennett [2] and others.[3]

## Diagnosis of Hypoadrenalism

Patients with hypoadrenalism who must undergo surgery may be classified into two categories. First, they may have adrenocortical insufficiency but their operation may be classified as elective. It can be put off until the appropriate time. Second, they may have adrenocortical insufficiency at a time when injury or disease requires an emergency operation. The diagnosis of hypoadrenalism in each of these cases is a difficult problem.

*Elective Cases.*—When faced with the problem of operating on a patient in whom he suspects adrenocortical insufficiency, the surgeon would like to know whether this condition actually is present. Adrenal insufficiency may not be provoked until a very major stress occurs, such as an operation of great magnitude. It also may occur, however, with a far less stressing incident, such as a simple manipulation of the knee with the patient under anesthesia.[4]

We have had difficulty in determining whether the patient who has been receiving steroids for some length of time is actually devoid of adrenocortical function. One of the indicators we have been studying is the measure of salt conservation after an intravenous infusion of corticotropin (ACTH). The amount of salt excreted in the urine per 24 hours is measured for 48 hours, during which time the salt intake is calculated and restricted to not over 3 Gm. per 24-hour period. During this time blood electrolytes as well as the 24-hour urinary potassium and sodium excretion are measured. After the 48 hours have passed, an infusion is given of 50 mg. of corticotropin in 500 cc. of dextrose and water over a 4-hour period. Thereupon, in the next 24 hours, at 12-hour and 24-hour periods, the total uri-

From the Hospital for Special Surgery, the Margaret Caspary Research Department, Cornell University Medical College.

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nary salt excretion is recorded as well as the blood electrolytes. If the patient has normal adrenal function, the amount of salt excreted in the urine in the 24 hours after this test will decrease by 50 to 75% of that in the control period. Since the average person normally excretes about 100 mEq. of salts a day per liter of urine, usually the excretion in the urine will not exceed 40 or 50 mEq. per liter over the 24 hours after the infusion. Therefore, if the amount excreted fails to decrease, this failure to conserve salt after the test with corticotropin should alert one to the possibility of hypoadrenalism. This condition is especially likely to exist if the patient also fails, after the infusion of corticotropin, to develop hypokalemia, a slight rise in the plasma level of 17-hydroxycorticoids, and a transient eosinopenia, all of which occur in the normal person. The absence of these particular changes in response to corticotropin provides a useful indicator that supportive steroid therapy may be required. Clinically, the presence of asthenia and hypotension is doubly significant, especially if the patient has received adrenocortical steroids for over three months.

We have used this method of assay in nine patients, and we have been able to demonstrate to our satisfaction, prior to surgery, the need for supplementary treatment during stress in six patients. The successful treatment of these six patients with supportive therapy indicates either that this method of assay was useful or that the administration of corticosteroids did not harm the patient in the recovery from stress even if the supplementary steroid was not actually needed. The three patients in whom the preliminary tests disclosed salt conservation after infusion of corticotropin, despite long-term treatment with cortisone, received no supplementary steroids and tolerated surgery without difficulty.

*Emergency Cases.*—A second problem, which is difficult to evaluate, occurs in the patient who must have emergency operation or treatment due to injury and in whom there may be some deficiency in pituitary or adrenal function. In this instance, one is not able to examine the patient elaborately prior to surgery, and, consequently, we have found that a regimen similar to that described recently by Perlmutter[5] has been of some help to us in the subsequent management. In such cases, where a history of cortisone therapy has been given, the simultaneous examination of a specimen of voided urine and of blood for sodium concentration will be useful. A high degree of salt excretion and a low serum sodium level should suggest the possibility of hypoadrenalism and alert the surgeon to the need for treatment in the event of shock. In emergency cases, the presence of eosinophilia, unexplainable hypotension, and a high urinary volume and salt excretion indicates adrenal insufficiency.

*Occurrence and Treatment of Adrenocortical Insufficiency in Ten Orthopedic Patients Undergoing Elective or Emergency Surgery*

| Case No. | Surgery | Age, Yr. | Sex | Diagnosis | Steroid Used Previously | Operation | Supplementary Management | Shock | End-Result, Time After Surgery |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Elective | 43 | M | Pemphigus, 2½ yr. (osteoporosis; avascular necrosis, hip) | Cortisone acetate, 35-1,000 mg. (av. 200 mg. daily) | Replacement of head of femur | Cortisone, salt, blood | 9 times in 72 hr. | Living and well, 4 yr. |
| 2 | Elective | 37 | M | Adrenal cortical hypofunction (Addison's disease); arthritis, lumbosacral and sacroiliac joints | Desoxycorticosterone acetate (Doca) pellets, 150 mg.; cortisone, 25 mg., 7 yr. | Spinal fusion and sacroiliac fusion; removal of plate (4 mo. later) | Desoxycorticosterone, cortisone, hydrocortisone I.V., saline solution, blood | none | Wound infection, living and well, 2 yr. |
| 3 | Elective | 60 | M | Rheumatoid arthritis; protrusio acetabuli | Cortisone, 75 mg., 18 mo.; hydrocortisone, 20 mg. (stopped 3 wk. prior to surgery) | Angulation-resection osteotomy, hip | Hydrocortisone I.V., cortisone, prednisone (Meticorten), blood | none | Living and well, 4 mo. |
| 4 | Elective | 36 | M | Rheumatoid arthritis (severe contractures) | Hydrocortisone, orally, 20 mg. daily, 2 yr. | Femoral osteotomy | Cortisone, hydrocortisone I.V., blood | none | Living and well, 18 mo. |
| 5 | Elective | 68 | F | Rheumatoid arthritis; intracapsular fracture, nonunion (osteoporosis) | Hydrocortisone orally, 20-40 mg., 4 mo. | Smith-Petersen nailing; Fred Thompson prosthetic replacement, 6 wk. later | Cortisone, hydrocortisone, prednisone, blood | twice | Living and well, 18 mo. |
| 6 | Elective | 54 | M | Rheumatoid arthritis; fracture of right hip, nonunion | Hydrocortisone; cortisone, 50-100 mg., 3 yr. | Prosthetic replacement, right hip | Hydrocortisone I.V., cortisone I.M., blood | none | Living and well |
| 7 | Emergency | 56 | M | Rheumatoid arthritis; ruptured appendix (fistula [fecal], sepsis, osteoporosis) | Cortisone, 50 mg. I.M.; hydrocortisone intra-arterially, 18 mo. | Appendectomy; closure evisceration (2 wk. later) | Hydrocortisone I.V., cortisone, saline solution, blood | 3 times in 24 hr. | Death (adrenal atrophy and sepsis) |
| 8 | Emergency | 78 | F | Rheumatoid arthritis (osteoporosis); intracapsular fracture of hip | Prednisone, 20 mg., 8 mo. | Smith-Petersen nailing of hip | Hydrocortisone I.V., cortisone, prednisone, blood | twice | Living and well, 6 mo. |
| 9 | Emergency | 78 | F | Idiopathic thrombocytopenic purpura; intracapsular fracture of hip; osteoporosis | Prednisone, 40 mg., 6 mo., 10-40 mg. | Knowles pins, hip | Cortisone, prednisone, blood | none | Death, 4 mo. (autopsy showed normal adrenals) |
| 10 | Emergency | 48 | F | Osteoarthritis; intracapsular fracture of hip | Prednisone, 20-30 mg., 9 mo.; hydrocortisone | Smith-Petersen nailing of hip | Prednisone, hydrocortisone I.V. | none | Living and well |

## Present Series

We have collected the data on 10 patients requiring operations on the bones and joints (see table). All of the patients had been receiving cortisone or other steroids for at least four months prior to surgery. One of them had also been receiving desoxycorticosterone acetate (Doca) pellets for seven years because of adrenal cortical hypofunction. Two of the patients had been receiving prednisone and two, hydrocortisone orally. Three additional patients were suspected of having adrenal insufficiency because of long-term corti-

sone therapy, but they did not demonstrate this condition in response to the test with corticcotropin. They are not included in this study.

It was of great interest to note the preoperative conditions that required treatment with steroids. Six persons were afflicted with rheumatoid arthritis of advanced degree, one had pemphigus, one had idiopathic thrombocytopenic purpura, one had adrenal cortical hypofunction, and one had been receiving cortisone for osteoarthritis. None of the patients had received corticosteroids for less than four months. Dosages ranged anywhere from 20 mg. of prednisone a day for four months to 1,000 mg. of cortisone a day over two years. Two patients died: one directly as a result of adrenal insufficiency and treatment, the other four months later of other causes. We have been able to examine the adrenals of both of these patients. The autopsy of the patient who died soon after operation disclosed adrenal atrophy, with both adrenals weighing less than 3 Gm. There were thin cortices, with loss of the lipid substance. However, in the patient with thrombocytopenic purpura who died four months after operation, the adrenals appeared normal despite the patient's having received heavy doses of prednisone for over six months up to the time of death.

Six of the patients thought to have induced hypoadrenalism underwent elective surgery and four underwent emergency surgery. Three of the four undergoing emergency surgery required open treatment for fractures, while the fourth, with arthritis, developed a silent ruptured appendix. Operative procedures performed on the patients included insertion of Knowles' pins and Smith-Peterson nails, spinal fusion, osteot-

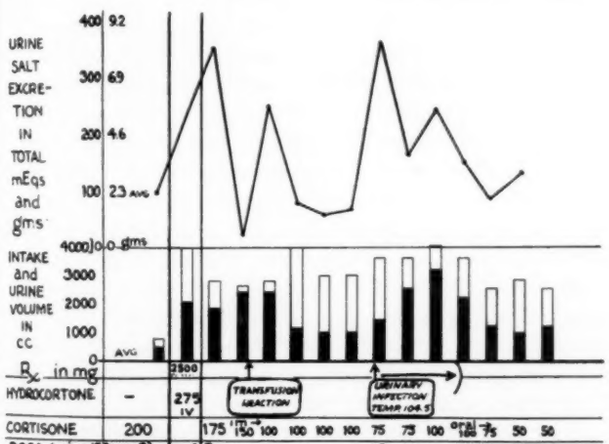


Fig. 1.—Salt loss and treatment in patient with adrenal cortical hypofunction (Addison's disease) undergoing spinal fusion.

omy, resection-angulation osteotomy, and prosthetic replacement of the head of the femur. The ages ranged from 36 to 78 years.

Treatment consisted of increasing the amounts given of steroids in various forms and, in some cases, of salt administration during surgical stress and shortly thereafter. One patient also received desoxycorticosterone. Details of management varied, depending on the particular time these patients were studied. For example, in 1952 a patient was carried through simply with intramuscular administration of cortisone every four hours and with salt, whereas the last patient was given cortisone intramuscularly before, hydrocortisone intravenously during, and prednisone after surgery. In only one case, because of adrenal cortical hypofunction, was it necessary to use desoxycorticosterone. In this patient, after a spinal fusion, a transfusion reaction and a urinary tract infection produced a sharp increase in salt excretion, requiring the use of additional desoxycorticosterone, salt, and cortisone. Figure 1 illustrates the rise in urinary salt excretion and the need for supplementary steroids in this patient.

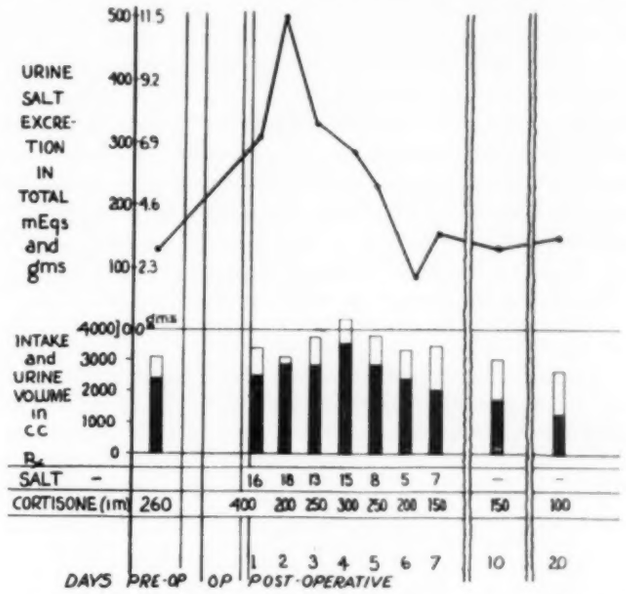


Fig. 2.—Salt loss and treatment in patient with induced adrenal insufficiency undergoing replacement of head of femur.

Follow-up of these patients varies from six months to four years. In no instance after convalescence has there been any evidence of further adrenocortical insufficiency. Except during periods of stress, practically all the patients were receiving low maintenance doses or no steroids whatsoever when last seen.

*Clinical Response During Early Postoperative Period.*—Shock occurred in 4 of the 10 patients postoperatively. (This was defined as blood pressure under 80/50 mm. Hg, pulse rate over 120 per minute, and clinical appearance of shock.) The first patient we studied, who had pemphigus, had nine separate bouts of shock within 72 hours postoperatively, requiring heroic, constant treatment. Undoubtedly, in this patient shock was due to frank insufficiency as well as to poor management. The fact that this patient's urinary salt excretion was excessive can be seen in figure 2. One patient died despite all attempts at therapy. Within three weeks this patient had had three separate bouts of shock. Death was due to sepsis and overwhelming infection as well as to adrenal atrophy. One patient, who had undergone an uncomplicated Smith-Petersen nailing, had two separate bouts of shock 24 hours after operation. A second patient had two separate bouts of shock within the first 24 hours after replacement of the head of the femur. The intravenous

use of hydrocortisone in both of the last-mentioned patients was effective in restoring blood pressure to normal. All of the patients operated on received adequate blood transfusions. In none of the patients was hemorrhage the cause of shock. Particular care was taken to maintain blood volume. It was interesting to note that in no instance was shock present while the patient was under anesthesia; it occurred only after the patient had awakened. The shock would come on in a matter of minutes and lasted, in one case, as long as two hours. Usually, marked improvement was noted within a half-hour after administration of hydrocortisone. In addition, each of the four patients in whom shock developed had eosinophilia and an unusually high salt excretion for a number of days after surgery. This, to us, was significant evidence that there was a defective adrenocortical response to the stress of surgery or injury. In no instance was there evidence of renal disease or water intoxication.

### Treatment

The hypotensive state may come when one expects it least, namely, during the first 24 to 48 hours postoperatively. It comes on with great speed and requires definitive treatment. One cannot wait for corroboration by the laboratory in such cases. The treatment of adrenocortical insufficiency with a corticosteroid is most important. Even if one is not certain in such an emergency that the hypotension is due to adrenal depletion, we feel that hydrocortisone should be given intravenously along with other supportive treatment. A high eosinophil count in the presence of severe stress (with a high amount of urinary salt excretion), as well as persistent tachycardia and hypotension despite adequate blood replacement therapy, is an indication that adrenocortical insufficiency is present. We feel that the treatment of induced adrenocortical insufficiency can proceed along three lines.

1. Patients undergoing emergency surgery should receive 100 mg. of hydrocortisone intravenously in 500 cc. of saline solution, supplementary blood, and cortisone intramuscularly in 50-to-100-mg. doses. 2. Patients undergoing elective surgery who require cortisone up to the time of surgery should be treated as follows: Preoperatively, they should receive 100 mg. of cortisone at 9 p. m. the evening before and at 7 a. m. the morning of operation. During operation, they should receive 100 mg. of hydrocortisone in addition to blood. Postoperatively, they should receive, every 12 hours, 50 to 100 mg. of cortisone the first day and 25 to 50 mg. the second day. Then, if the course is satisfactory, prednisone should be substituted on the third day and given daily in 20-mg. doses for three days, and the doses should then be tapered off. 3. For patients undergoing elective surgery who do not require steroids, the surgery should be put off for three months while steroid administration is tapered off and the patient's adrenal function is studied.

Response to the first two regimens described indicates that the assumption of adrenocortical insufficiency is correct, although actual proof of this may be difficult. However, we feel that, since it is only a short-term method of treatment bolstered by continuing intramuscular administration of steroids, the danger of infection or failure in wound healing is quite remote. This is particularly true in operations on extremities, where sepsis is less catastrophic, rather than in operations on the intestine. However, high doses of cortisone will interfere with repair, and, therefore, one should take the patient off this regimen as quickly as possible.[6] In this particular series, infection occurred in only one patient, when pyelitis, cystitis, and wound infection developed in the patient with adrenal cortical hypofunction.

Long-term prednisone therapy did not produce pathologically detectable adrenal atrophy in the patient with idiopathic thrombocytopenic purpura, who came to autopsy. Whether functional atrophy was present is not known, as this patient was operated on for a fracture and was not studied preoperatively.

### Summary and Conclusions

There are a great many steroids on the market today that may cause adrenocortical insufficiency if they have been used for a long time prior to surgery. It is important to know whether adrenocortical insufficiency occurs, as it produces shock and is easily manageable. Therefore, each patient should be closely questioned for pretreatment with a corticosteroid. The use of a salt-excretion test after infusion of corticotropin has been of some value preoperatively as an indicator of adrenocortical insufficiency and, thus, of the need for supplementary treatment.

Ten patients who had been receiving cortisone acetate for a sufficient amount of time to produce in some of them adrenocortical insufficiency underwent operation. In six of nine patients in whom a preoperative test with corticotropin was utilized, the failure to conserve salt in addition to the failure to develop eosinopenia indicated the need for supportive therapy, and these patients were managed on such a program during surgery with a minimum of discomfort. One patient on long-term corticosteroid therapy did not present evidence of adrenocortical insufficiency at autopsy, while still another did produce evidence of this. Accordingly, adrenocortical insufficiency often, but not always, results from prolonged administration of steroids.

One should test for adrenocortical insufficiency rather than take its presence for granted prior to surgery. Operations on any patients undergoing elective procedures on the bones and joints should be postponed, therefore, until an assay to rule out adrenocortical insufficiency has been undertaken. A patient who has been receiving cortisone or another corticosteroid for any length of time and who requires surgery should be weaned away from the steroid for several months and then have surgery performed. When a patient has been receiving cortisone, however, because of other factors and when emergency surgery is required, treatment should consist of administration of increased amounts of cortisone and hydrocortisone during and after surgery, as needed, until the patient's condition becomes stable.

110 E. 87th St. (Dr. Nicholas).

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Dr. Robert Kaufman, New York, gave permission to report case 9.

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# THE NATURAL HISTORY OF HERPES ZOSTER


**Carroll F. Burgoon Jr., M.D., Jane S. Burgoon, M.D., Philadelphia**
and
**G. Douglas Baldridge, M.D., Los Angeles**



*• The course of herpes zoster was studied in a series of 206 patients that included infants and octogenarians. There were 32 patients under the age of 20; in 30 of these (94%) the condition cleared up in 14 days or less. The infection was more severe and prolonged in older patients. In four elderly patients symptoms persisted six months or longer. The relative frequency with which the various parts of the nervous system were involved varied from youth to old age. No instance of involvement of the ophthalmic division of the trigeminal nerve was observed in patients under the age of 20, but ocular complications did not appear to be related to the aging process. Postherpetic neuralgia did not occur in patients under 20 but was frequent in patients over 50. Sex, race, and season did not perceptibly influence the incidence of infection in this series.*


Herpes zoster is an acute, self-limited disease of infectious origin. It is characterized by grouped vesicular lesions on an erythematous base distributed over several dermatomes as well as, in some cases, by a systemic reaction. This study of the incidence, duration, distribution, and complications was undertaken to establish clearly the natural history of the disease. Impressions gained from the more severe reactions associated with herpes zoster have tended to color the picture unfavorably. As a result of these impressions, the literature is crowded with many reports of treatments advocated to alleviate pain and shorten the course of the infection. Jadassohn [1] suggested the benign nature of herpes zoster in his review, but, until recently, no attempts have been made to chart its natural course. It is hoped that this study will serve as a yardstick to evaluate the future claims for therapeutic success in patients with this infection.

The majority of the 206 cases for this analysis were chosen from the dermatology and ophthalmology departments of a general hospital (Hospital of the University of Pennsylvania, Philadelphia) and the outpatient department of a pediatric hospital (Children's Hospital of Philadelphia) over a 15-year period. By surveying a pediatric hospital and an ophthalmology clinic, we naturally increase the number of children and the incidence of ophthalmic involvement. We felt that this would give a more valid picture of the infection than a study of cases selected from a dermatology clinic alone, and that this was a valid assumption is shown by a comparison of the age groups in our series with the percentage of the population of Philadelphia in the various age groups.

In analysis of the data, the number of cases in the study of any one facet of the infection varies according to the information that was available on the various cases. The infection was considered to have cleared when all crusts had fallen off leaving erythematous, macular lesions. The postinfectious inflammatory reaction on the skin was not considered part of the acute infection in the evaluation of the length of the infection. Neuralgia following herpes zoster was defined as any subjective, painful sensation that persisted after the acute phase of the infection. Treatment consisted of a number of nonspecific measures and, therefore, did not enter into the data.


From the Department of Dermatology, Hahnemann Medical College of Philadelphia (Dr. C. F. Burgoon); the Visiting Staff, Children's Hospital of Philadelphia (Dr. J. S. Burgoon); and the Department of Dermatology, University of Southern California School of Medicine (Dr. Baldridge).



Read before the Section on Dermatology at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.


## Etiology

Virological studies have established clearly the similarity of the infectious agents in chickenpox and herpes zoster. The elementary bodies seen under the electron microscope are rounded or brick-shaped and measure approximately 210 by 243 mμ. They are most numerous during the first 12 to 24 hours and decrease rapidly, so that by 72 hours they are practically nonexistent. The virus particles from chickenpox and herpes zoster are indistinguishable in all physical appearances. Von Bokay [2] suggested the close relationship between the two after observing cases of chickenpox arising after contact with herpes zoster. Since then, many reports of chickenpox occurring in persons who are in contact with patients with herpes zoster have been reported, while the reverse has been much less commonly observed. In this connection, the British medical research council reported 20 outbreaks of chickenpox instituted by cases of herpes zoster in boarding schools for boys during a five-year period.

Kundratitz [3] and Bruusgaard [4] have observed that the intradermal injection of fluid from fresh vesicles of herpes zoster in children under 6 years of age will produce localized lesions of clinical chickenpox in 9 to 12 days after inoculation. All adults and children with a previous history of chickenpox fail to develop lesions after inoculation. Complement-fixation reactions with herpes zoster fluid or chickenpox crusts as an antigen and convalescent serum show cross fixation of complement between the two diseases. In addition, convalescent serum produces cross agglutination of elementary bodies under the electron microscope.

Herpes zoster is classified as spontaneous (primary) or symptomatic (secondary) depending on whether or not there is a predisposing factor. The majority of cases are of the primary variety, in which no known causative factor triggers the infection.

In this series, one case of herpes zoster was associated with a lymphoblastoma. In addition, symptomatic (secondary) herpes zoster has been recorded occurring after a variety of traumas; these include spinal puncture, intramuscular injections, x-ray therapy, and administration of arsenic. The present study does not suggest a statistically valid correlation with any trigger mechanism. However, the possibility that traumatic factors may activate a latent virus is suggested by the observation of 16 cases of herpes zoster among 406 patients with carcinoma of the breast (12 of the 16 had metastases).[5]

No information concerning the incubation period of the virus was obtained from the analysis of the data. The most valid information concerning this is provided by the human inoculation experiments in which a period of 7 to 14 days elapsed between the injection of herpes zoster fluid and the production of a reaction.[6]

## Clinical Picture

Herpes zoster infections may generally be divided into three general groups, according to the symptoms: (1) those associated with involvement of the cutaneous system; (2) those associated with involvement of the nervous system; and (3) those associated with a generalized systemic response to the infection.

The skin lesions typically appear first as erythematous papules, which progress to vesicles within 12 to 24 hours and to pustules in 72 hours. When pustulation appears, the surrounding erythema begins to subside, and in seven to eight days the pustules begin to dry. Crust formation occurs in 10 to 12 days, and the crusts fall off in 2 to 3 weeks. In very mild infections, the cutaneous lesions may remain as erythematous maculopapules and rapidly regress within 7 to 10 days without vesicles appearing. In an occasional case, the cutaneous reaction is so severe that the lesions become gangrenous and weeks are required for complete healing. The cutaneous reaction characteristically involves one or more dermatomes spreading in a band-like manner. Unilateral segmental involvement is the rule, although bilateral involvement does occur. The latter occurred in less than 0.5% of the cases in this series. The grouped vesicles frequently appear on the skin over the proximal portion of the involved nerve root and spread distally. The thoracic segments are most frequently involved, but any area of the skin or mucous membrane may be affected.

Involvement of the nervous system was associated with some variety of pain in 66% of the patients in this study. The pain associated with the infection may appear as a prodromal symptom, during the acute infection, or after the inflammatory reaction on the skin has subsided. It is usually categorized by the patient as pruritic, stabbing, burning, or aching in nature and can be constant or intermittent. The pain is evanescent in most patients but is quite persistent in others and seems to bear no relation to the severity of the skin involvement. Prodromal pain is not uncommon four to five days prior to the skin changes, but occasionally a segmental burning pain lasts for 10 to 14 days without obvious skin lesions. On close inspection, a faint macular erythematous eruption may be seen as the only cutaneous manifestation, although the regional lymph nodes are usually enlarged and tender.

Systemic response to the infection usually consists of headache, malaise, nausea, temperature elevation, stiff neck, and regional lymphadenopathy. In this study, a systemic reaction was observed in 5.8% of the cases. In our experience, this type of response is more common in the pediatric age group; only one of our patients with this reaction was an adult.

Two patients gave a history of previous episodes of herpes zoster, one occurring in the same distribution. Interpretation of the history is difficult because of the occasional tendency of herpes simplex infection to have a zosteriform distribution. Four patients (2%), aged 55, 62, 72, and 82 years, developed a generalized vesicular eruption. The eruption was associated with different segments (ophthalmic, cervicothoracic, lumbar). The vesicles appeared over a 48-hour period in two patients and cleared in two weeks, while in the third patient, aged 72 years, the vesicles appeared over a seven-day period and the eruption required five weeks to clear. From this study, we conclude that herpes zoster generalisatus is uncommon and appears to be most frequent in older age groups.

## Incidence

We have made no attempt to evaluate the percentage of cases of herpes zoster in the total number of admissions to a dermatology clinic. We suspect, however, that the infection is significantly more common than the reported frequency of 0.5 to 2%. The layman can easily make the diagnosis, and many persons with the disease never seek medical care.

Results similar to those that we would expect in a study of the true incidence of herpes zoster infection were obtained in the study of the incidence of herpes simplex in 1,000 families. In that study,[7] the actual incidence of apparent infection in the families studied was found to be 15%, in contrast to less than 1% incidence in the total number of patients seeking medical care in an outpatient study.

*Climate.*—No climate nor country seems to be free from herpes zoster. Some reports have suggested a seasonal variation in the incidence of infection. In an analysis of our cases, we found no statistically valid

difference in incidence in any of the four seasons. Simons [8] was unable to show any climatic influence in an extensive study on the incidence of infection in Europe and the tropics.

*Sex.*—Some studies have suggested that the infection is slightly more common in males than in females, but this series shows no significant difference in incidence. Of the 206 patients, 50.7% were males and 49.3% females as compared with the total population in Philadelphia of 48.3% male and 51.7% female.

*Age.*—In all previous studies in which the relation between age and frequency of infection were considered, the incidence of infection fell off markedly after the age of 60. However, when the incidence in various age groups is correlated with the population distribution in those age groups, our study indicates that this apparent decrease with increasing age is actually an increase (fig. 1).

*Race.*—Our study would indicate that there is no apparent difference in incidence of the infection in white and nonwhite population. One might expect that, since this is a study of clinic patients in Philadelphia, there would be an overly large number of patients in one group; however, correlation of our group with the percentage of population in each group in the city of Philadelphia shows that we had a normal racial distribution among our patients. Of 111 patients, 81.8% were white and 18.1% were nonwhite as compared with the total population of Philadelphia of 81.9% white and 18.2% nonwhite.

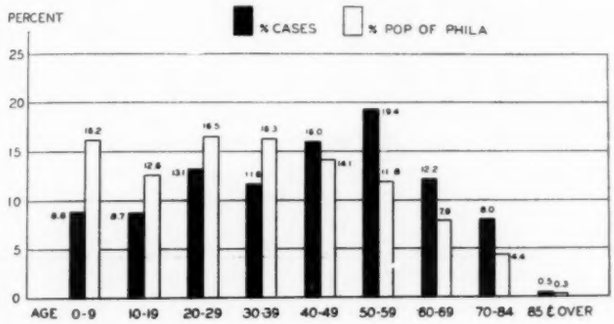


Fig. 1.—Incidence of herpes zoster by age groups compared with Philadelphia population distribution in each group.

### Appearance and Distribution of Vesicles

The severity and duration of an infection can be postulated if one observes the number of days over which new vesicles appear. Generally, the crusts fall off in from two to three weeks, depending upon the severity of the local destruction. In our group of 206 cases, the local reaction was so severe in two cases as to produce a superficial type of gangrene. Both of these patients were 60 years old and had no known systemic disease.

Of this series of patients, 156 were analyzed as to the number of days over which crops of vesicles appeared. In 26.1% of the cases, all of the vesicles appeared within the first 24 hours; in 35.9%, in 48 hours; in 12.9%, in 72 hours; and in 12.9%, in 96 hours; in the remainder they continued to appear up to as long as seven days. There was good correlation with the duration of the lesions in that (1) if all of the vesicles appeared in the first 24 hours, the eruption cleared in 10 to 13 days; (2) if they all appeared in the first 48 hours, the eruption cleared in 14 to 16 days; and (3) if the vesicles continued to appear for seven days, the eruption continued up to five weeks (fig. 2).

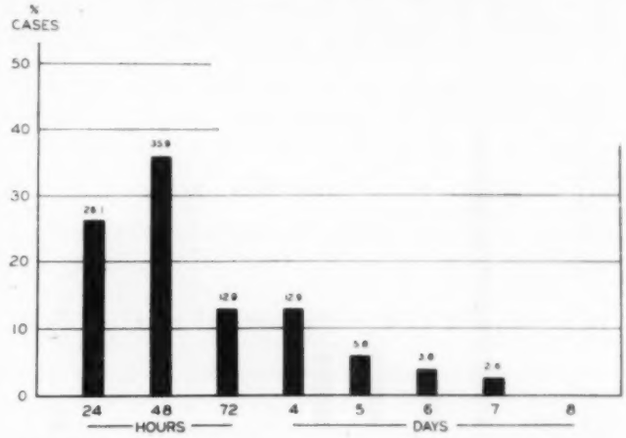


Fig. 2.—Periods of time and percentage of cases (156) in each period within which all vesicles appeared.

In 183 cases, the relation of age to the severity of the cutaneous reaction was studied to determine whether they were significantly related and whether age influenced duration. There were 32 patients in the infant-to-19-year age group. Of these, the lesions of 30, or 94%, cleared in 7 to 14 days. There were 70 patients in the 40-to-59-year age group. Of these, the lesions of 34, or 49%, cleared in 7 to 14 days; 9, or 13%, in 15 to 20 days; 15, or 21%, in 21 to 28 days; and 8, or 11%, in 29 to 55 days; the lesions of the remaining 4, or 6%, lasted longer than 55 days (fig. 3). From these figures, it can be seen that the severity of the infection is greater in the older age groups and that, therefore, the duration is longer.

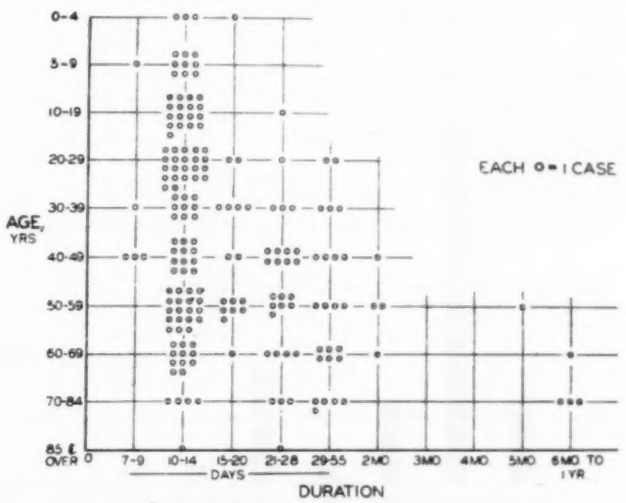


Fig. 3.—Duration in days and months from onset to clearing of all symptoms of herpes zoster in 183 patients in various age groups.

### Duration and Distribution

The duration of the infection was determined in 183 cases wherein the duration of the infection was considered to be the period from onset to clearing of all symptoms. In this group, 163 patients, or 89.1%, were clear of all skin lesions within five weeks. Of these 163, the condition in 2.7% cleared in 7 to 9

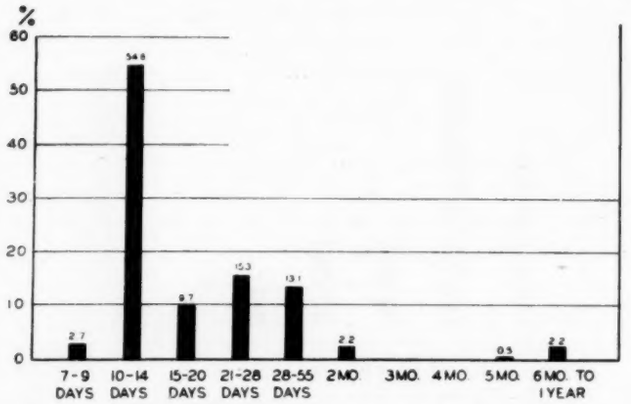


Fig. 4.—Duration in days and months from onset to clearing of all symptoms of herpes zoster and percentage (of 183 cases) in each duration period.

days; in 54.6%, in 10 to 14 days; in 9.7%, in 15 to 20 days; in 15.3%, in 21 to 28 days; and in 6%, in 28 to 35 days (fig. 4). The remaining 20 patients, or 12%, had pain that persisted after the crusts had fallen off.

A number of reports have indicated the approximate frequency of the sites involved by herpes zoster. Although they all agree as to the frequency of distribution, none has related the frequency of the site of involvement to the age groups. We analyzed 204 cases for frequency of distribution and correlated the distribution with age.

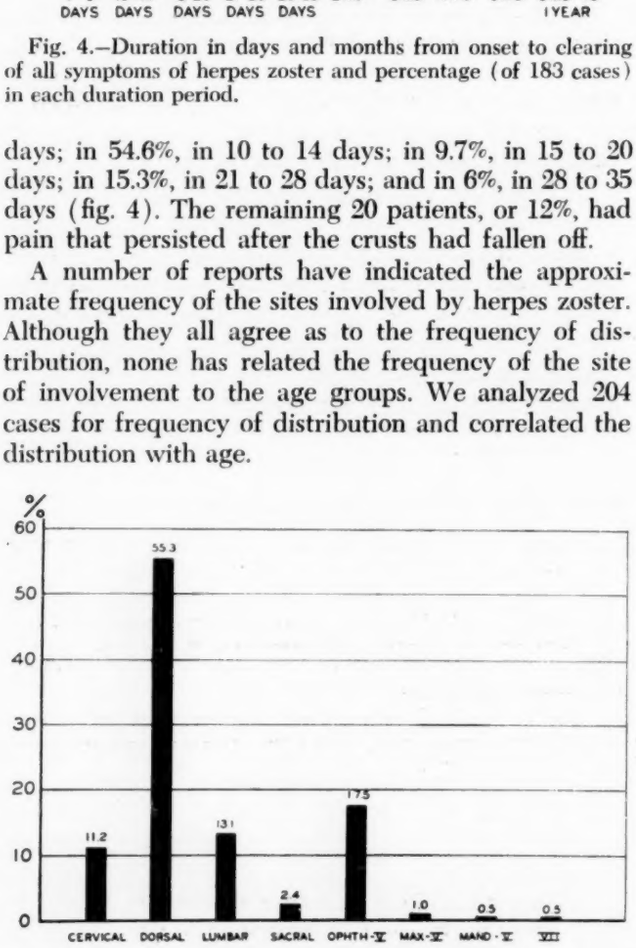


Fig. 5.—Data from 206 cases on distribution of herpes zoster in regard to involvement of nervous system.

The data on distribution in regard to involvement of the nervous system were essentially in agreement with data in previous studies: cervical, 11.2%; thoracic, 55.3%; lumbar, 13.1%; sacral, 2.4%; ophthalmic, maxillary, and mandibular divisions of the fifth cranial (trigeminal) nerve, 17.5%, 1.0%, and 0.5% respectively; and the seventh cranial (facial) nerve, 0.5% (fig. 5). The high incidence of ophthalmic involvement is at variance with other studies but can be accounted for by the inclusion of the cases from the eye clinic. In this analysis, cervicothoracic and lumbosacral were recorded under each distribution. There were four patients with cervicothoracic, one with lumbosacral, and none with thoracolumbar involvement.

Since age appeared to play a part in the site of involvement, the distributions in the age groups between infancy and 19 years and between 40 and 59 years were analyzed. In the 37 patients under 20 years of age, the nerve involvement was either lumbar or thoracic in 89%, cervical in 3%, and maxillary in 1% (fig. 6). In the 75 patients in the 40-to-59-year age group, the involvement was either lumbar or thoracic in 65.4%, cervical in 10.7%, sacral in 1.3%, ophthalmic in 20%, maxillary in 1.3%, and mandibular in 1.3%.

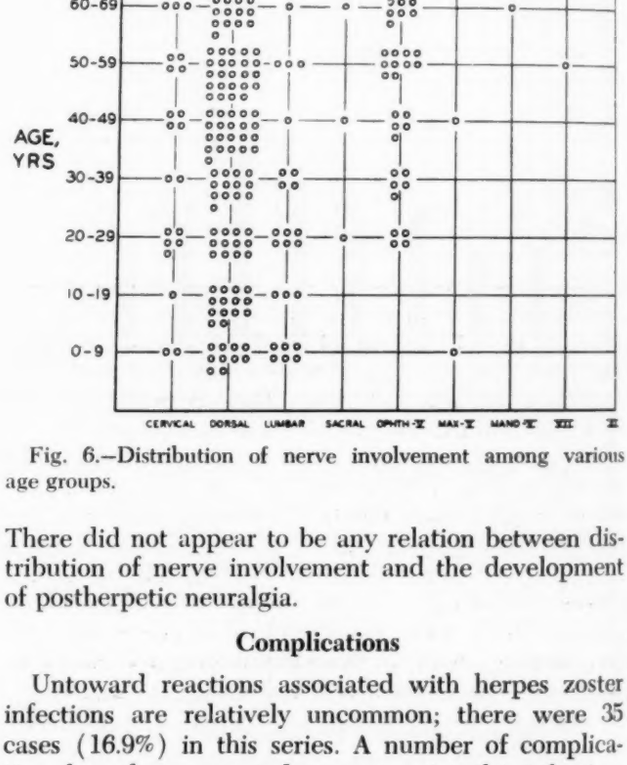


Fig. 6.—Distribution of nerve involvement among various age groups.

There did not appear to be any relation between distribution of nerve involvement and the development of postherpetic neuralgia.

### Complications

Untoward reactions associated with herpes zoster infections are relatively uncommon; there were 35 cases (16.9%) in this series. A number of complications have been reported accompanying this infection. They are as follows: a superficial type of gangrene, postherpetic neuralgia, endocarditis, meningoencephalitis, paralysis of motor nerves, corneal ulcers, keratitis, and iritis.

In our study, postherpetic neuralgia was the most common complication, occurring in 20 cases (9.7%). This is a rare problem in the patient under 40 years of age. It occurred in only one patient in the 20-to-29-year age group and lasted only six weeks. The distribution of the remaining 19 cases of postherpetic neuralgia and the duration of the disorder were as follows: (1) 40-to-49-year age group, one (5%), lasting two months; (2) 50-to-59-year age group, four (20%), lasting two, three, four, and six months respectively;

(3) 60-to-69-year age group, seven (35%), with one lasting one month; two, two months; three, three months; and one, six months; (4) 70-to-85-year age group, six (30%), with one lasting one month; two, two months; and three, six months or longer; and (5) over 85, one (5%), lasting six months (fig. 7). Thus the incidence of this complication increases with increasing age, particularly when the population distribution is taken into account.

The ophthalmic division of the fifth cranial nerve was involved in 36 (17.5%) of the 206 patients in this study. Complications such as iritis, conjunctivitis, keratitis, and extraocular muscle paralysis occurred in 12 patients (5.8%). It can be seen that complications associated with this particular segmental distribution were more common than complications arising from

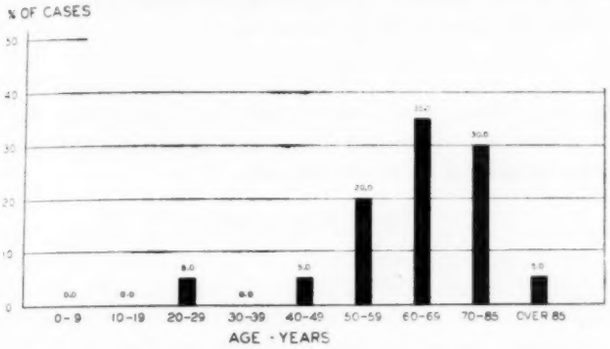


Fig. 7.—Distribution, percentagewise, in various age groups of 20 cases of postherpetic neuralgia.

any other one group—33.3% in a total of 36 cases. The most common ocular manifestation was conjunctivitis, occurring in 7 (19.4%) out of 12 of the 36 patients with ophthalmic herpes zoster. Keratitis with or without ulcer occurred in an additional three patients (8.4%), while iritis and extraocular muscular paralysis occurred in one patient each (2.8%). The paralysis in the 48-year-old patient with extraocular muscular paralysis cleared within four months. Neuralgia occurred in three of these patients, aged 65, 72, and 78. Ocular complications did not appear to be related to the aging process. There was 1 (8.3%) of the 12 patients with such complications in the 20-to-29-year age group and there were 2 (16.6%) in the 30-to-39-year age group, 4 (33.3%) in the 40-to-49-year age group, 3 (25.0%) in the 50-to-59-year age group, and 2 (16.6%) in the over-60-year age group.

A superficial type of gangrene occurred in two patients, aged 60, or 1% of the total 206 patients studied. There was one case of meningoencephalitis in a 3½-year-old child, whose cerebrospinal fluid showed 376 white blood cells, with 40% polymorphonuclear cells and 60% lymphocytes, and normal chloride, protein, and sugar values. Electron microscopy of the spinal fluid did not disclose any elementary bodies. Another patient, aged 52, with geniculate ganglion involvement had a normal cerebrospinal fluid examination. Three patients had corneal ulcers.

## Summary

In order to determine the natural history of herpes zoster infection, 206 unselected cases of the disease were analyzed. From the analysis of these cases, we conclude that the following facts are significant: Age is an important factor, influencing the frequency of the infection, distribution of lesions, severity of cutaneous reaction, and incidence of postherpetic neuralgia. Ocular complications do not appear to be related to the aging process. Sex, race, and season do not influence the incidence of infection. A review of the present knowledge of morphology, immunology, and the clinical picture suggests a similarity of the viruses of herpes zoster and chickenpox.

2026 Delancey Pl. (3) (Dr. C. F. Burgoon).

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**Laryngeal Tuberculosis.**—The occurrence of laryngeal tuberculosis had been of grave prognostic significance prior to the days of antibiotic therapy. Now, due to the excellent response to antibiotics, laryngeal tuberculosis is merely a complication although it usually indicates a more severe variety of pulmonary tuberculosis, with breakdown of host resistance. . . . The treatment of laryngeal tuberculosis is essentially that of the parent condition, namely, pulmonary tuberculosis. Tuberculosis of the larynx responds very well to antibiotic therapy, using a combination of the known effective antituberculosis drugs. Healing is brought about in a great majority of cases in about four months but treatment is continued for at least one year and is stopped only if the pulmonary status is satisfactory. Effective drugs presently used are streptomycin, dihydro-streptomycin, isoniazid and PAS. Apart from voice rest, local therapy is now rarely used.—L. M. Arnold, M.D., Management of Tuberculosis of the Larynx, *Journal of the Mount Sinai Hospital*, July-August, 1956.

# CORTICAL EFFECT OF ALPHAPRODINE AND OF CHLORPROMAZINE DURING THIOPENTAL NARCOSIS

Valentino D. B. Mazzia, M.D., Alan Van Poznak, M.D.
and
Joseph F. Artusio Jr., M.D., New York

• *Although the exact mechanism is unknown, the administration of alphaprodine and possibly chlorpromazine can produce more satisfactory operating conditions when the patient is under light narcosis with thiopental. When the alphaprodine was administered, previously restless patients became quiet and stimulation of the skin and venipuncture no longer caused motion or withdrawal; at the same time, a decreased amount of thiopental was needed to produce the desired clinical response.*

A vast number of surgical procedures have been conducted with the patient under narcosis with thiopental sodium. The use of this thiobarbiturate has many clinical advantages, but the drug does lack a true analgesic quality, and the amount of this agent required to provide adequate operating conditions varies widely from patient to patient. Prolonged somnolence is an occasional undesirable result.

These disadvantages may be somewhat overcome when thiopental is used in conjunction with an analgesic such as alphaprodine (Nisentil) hydrochloride or a thalamic blocking agent such as chlorpromazine, with the result that a form of balanced anesthesia is obtained.[1] Laborit and co-workers,[2] Forster and co-workers,[3] Wallis,[4] and Kiersey and co-workers,[5] have stated that the addition of these drugs or similar agents can reduce the thiopental requirement by as much as one-third.

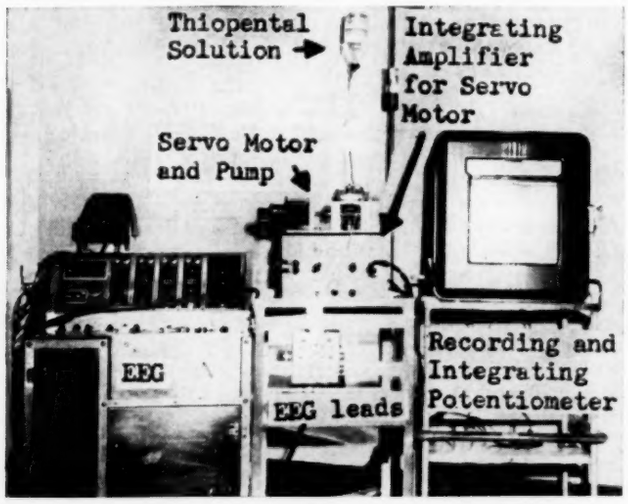


Fig. 1.—Apparatus used for study. Frontocentral needle leads connect to terminal board, which is connected to electroencephalograph. Amplified electrical impulses pass to integrating amplifier, which filters and integrates activity of 24 cps, driving the servomotor and pump assembly. Thiopental solution from reservoir is delivered at rate appropriate to maintain level of anesthesia in accordance with reference level previously selected on amplifier. Thiopental solution is thus delivered according to patient's needs, as determined by cortical electroencephalogram. A recording and integrating potentiometer measures the instantaneous flow and amount per time unit of thiopental administered.

The purpose of this study is to determine the effect of alphaprodine, levallorphan, and chlorpromazine on the electroencephalographic pattern and on the rate of thiopental administration during thiopental narcosis regulated by a servomotor.

From the Department of Surgery (Anesthesiology), the New York Hospital and Cornell University Medical College.

Read before the Section on Anesthesiology at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

## Method of Study

Seven patients were included in the study. Physical examination revealed no significant central nervous system, cardiovascular, or respiratory disease. Surgical procedures were limited to those on the lower extremities or on the lower part of the abdomen (table 1). Four patients received adequate subarachnoid block of the surgical field, adjusted to last at least throughout the duration of the procedure, with tetracaine hydrochloride–dextrose–epinephrine. Ephedrine was included in the procaine solution used for the skin wheal. Subarachnoid block was done in order to prevent sensory stimuli from interfering with the experimental method. In three patients, observations were made prior to surgery and no subarachnoid block was done.

Since the servomechanism was not capable of rapidly inducing anesthesia with a dilute solution of thiopental but could easily maintain any desired level of anesthesia, a priming dose of a 2.5% solution of thiopental was given by the anesthesiologist in order to place the patient at the desired level of narcosis as shown on the electroencephalogram. Frontocentral electroencephalographic needle leads were then inserted, and recordings were made on a Grass electroencephalograph, model III-D. An integrating amplifier filtered for activity of 24 cps received the amplified electrical impulses from the electroencephalograph and activated a servomotor, which in turn drove a modified American Optical blood pump. This apparatus delivered a 1 or 2% solution of thiopental at a rate to maintain a constant electroencephalographic reading of level 2 narcosis.[5] A recording and integrating potentiometer was included in the circuit to indicate the instantaneous rate and minute-by-minute volume of thiopental administered.

This servomechanism used for the automatic administration of an anesthetic agent (fig. 1) is similar to the one used for administration of cyclopropane previously described by one of us and co-workers.[6]

The mechanism has been modified for the administration of thiopental by the substitution of a pump activated by the servomotor for the valve control for cyclopropane and by the substitution of a circuit sensitive to the rate of administration of a solution rather than to the position of a flowmeter valve. Ventilation was adequately assisted by the administration of 100% oxygen by a face mask, with closed-circuit carbon dioxide absorption to prevent the development of hypoxia and hypercapnia. A stabilization period ranging from 15 minutes to one hour was then permitted until the electroencephalographic pattern and the rate of administration of thiopental became constant.

TABLE 1.—*Thiopental Requirements in Seven Patients Under Level 2 Narcosis Regulated by Servomotor*

| Case No. | Sex | Age, Yr. | Type of Procedure | Duration of Procedure, Hr., Min. | Premedication, Mg. | Spinal Anesthetic | Thiopental Priming Dose, Mg. | Servomotor Stabilization Period, Min. | Total Time on Servomotor, Hr., Min. | Thiopental, Mg./Min. | Total Dose of Thiopental, Gm. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 61 | Phlebectomy | 1,45 | Phenobarbital sodium, 90 Atropine, 0.3 | Yes | 300 | 15 | 1,7 | 22.4 | 1.5 |
| 2 | F | 43 | Repair of vesicovaginal fistula | 7,30 | None | Yes | 250 | 20 | 2,50 | 10.3 | 1.65 |
| 3 | F | 34 | Cystopexy | 2,0 | None | Yes | 500 | 15 | 2,6 | 10.3 | 1.3 |
| 4 | F | 37 | Presurgery | ... | Phenobarbital sodium, 130 Atropine, 0.4 | No | 500 | 15 | 2,30 | 16.7 | 2.5 |
| 5 | F | 43 | Presurgery study | ... | None | No | 875 | 30 | 0,43 | ... | ... |
| 6 | F | 46 | Presurgery study | ... | None | No | 400 | 25 | 1,40 | 17.5 | 1.75 |
| 7 | M | 17 | Phlebectomy | 2,0 | None | Yes | 450 | 75 | 2,0 | 50.4 | 6.05 |

TABLE 2.—*Effects of Intravenous Administration of Alphaprodine, Levallorphan, and Chlorpromazine in Seven Patients Under Level 2 Narcosis with Thiopental*

| Case No. | Other Effects of Alphaprodine* | Levallorphan, Mg.† | Other Effects of Levallorphan | Chlorpromazine, Mg.‡ | Other Effects of Chlorpromazine | Time Required to Recover Consciousness |
|---|---|---|---|---|---|---|
| 1 | Decrease in depth of respiration | 1 | Return of depth of respiration | 4 | Fall in blood pressure, tachycardia | 4 hr. |
| 2 | None | 1 | None | 4 | Fall in blood pressure, tachycardia | 35 min. |
| 3 | Apnea | 1 | Spontaneous respiration | 5 | Rise in blood pressure, tachycardia | 1 hr. |
| 4 | None | 1 | None | None | ... | Preoperative study |
| 5 | None | ... | ... | None | ... | Preoperative study |
| 6 | Apnea, no response to venipuncture | 2, in 2 doses | Spontaneous respiration | 5 | None | Preoperative study |
| 7 | Apnea | 1 | None | 5 | Fall in blood pressure, tachycardia | 2 days, in spite of light narcosis shown by EEG |

* 60 mg. of alphaprodine was administered to each patient, with no effect on the thiopental requirement.
† Administration of levallorphan had no effect on thiopental requirements.
‡ Administration of chlorpromazine had no effect on thiopental requirements.

The drugs under investigation were then given. Sixty milligrams of alphaprodine was administered intravenously. Fifteen minutes later, 1 mg. of levallorphan, a narcotic antagonist, was administered intravenously. Fifteen minutes later, an intravenous dose of 4 or 5 mg. of chlorpromazine was given. After 15 minutes of observation, an additional dose of thiopental was given rapidly into a vein other than the one used by the servomechanism and the effect was noted.

## Results of Study

After a priming dose of thiopental ranging from 250 to 875 mg., a 1 or 2% solution of thiopental was administered by the servomotor to maintain an electroencephalographic reading of level 2 narcosis. The administration of an average of 21.3 mg. of thiopental per minute was required, with a range of 10.3 to 50.4 mg. per minute. The general condition of the patients at this time was as follows: There was spontaneous respiration, noxious stimulation or venipuncture caused withdrawal flexion reflex, and occasionally there was spontaneous motion. Blood pressure and pulse were stable at the levels normal for each patient. The results are summarized in tables 1 and 2. Also see figures 2 and 3.

*Alphaprodine.*—Alphaprodine, 60 mg. given intramuscularly at a rate of 30 mg. per second, had no effect on the electroencephalographic pattern or on the rate of thiopental administration. However, there were marked clinical changes. Previously restless patients became quiet. Stimulation of the skin and venipuncture no longer caused motion or withdrawal. In three of the patients, apnea resulted and in one, a decrease in respiratory depth.

*Levallorphan.*—Levallorphan, 1 mg. given intravenously at a rate of 0.5 mg. per second, had no effect on the electroencephalographic pattern or on the rate of thiopental administration in five patients. After receiving levallorphan, two patients who had had apnea resumed spontaneous respiration and one patient with decreased depth of respiration resumed full activity. Two doses of 1 mg. each failed to restore spontaneous respiration in one patient. No other effects of the administration of levallorphan were noted.

*Chlorpromazine.*—Chlorpromazine, 4 or 5 mg. given intravenously at a rate of 2 to 2.5 mg. per second, had no effect on the electroencephalographic pattern or

on the rate of thiopental administration in five patients. In four of the five patients tachycardia averaging 34% was noted, and in three of the five patients there was an average fall in blood pressure of 48 mm. Hg systolic and 23 mm. Hg diastolic. After the effect of chlorpromazine was observed for 15 minutes, a dose of thiopental ranging from 100 to 250 mg. was

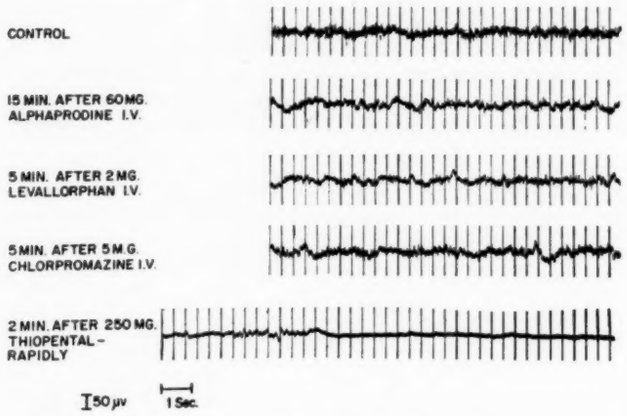
CONTROL
15 MIN. AFTER 60 MG. ALPHAPRODINE I.V.
5 MIN. AFTER 2 MG. LEVALLORPHAN I.V.
5 MIN. AFTER 5 M.G. CHLORPROMAZINE I.V.
2 MIN. AFTER 250 MG. THIOPENTAL - RAPIDLY
150 μv
1 Sec.

Fig. 2.—Effect of alphaprodine, levallorphan, chlorpromazine, and additional thiopental on electroencephalographic pattern during light anesthesia with thiopental. Cortical electroencephalogram is unchanged by administration of first three drugs, despite change in clinical condition (see text). Administration of additional thiopental, however, causes deeper level of anesthesia as seen on electroencephalogram.

administered rapidly through a vein other than the one used by the servomechanism. This produced an electroencephalographic pattern characteristic of a deeper level of narcosis and a decrease in the administration of thiopental by the servomotor.

## Comment

The administration of alphaprodine, levallorphan, and chlorpromazine does not alter the cortical electroencephalographic pattern when the patient is under light narcosis with thiopental, nor does it modify the amount of thiopental required for the servomechanism to maintain an electroencephalographic reading characteristic of light narcosis. The administration of alphaprodine and possibly chlorpromazine can produce more satisfactory operating conditions when the patient is under light narcosis with thiopental, but these drugs do not accomplish this goal by the potentiation of the cortical-depressant action of thiopental. Rather, these drugs act at sites as yet unknown.

The validity of the servomechanism should be discussed at this point. That the servomechanism is valid for administering thiopental has been shown by the fact that the manual administration of an extra dose of thiopental produces a deeper level of narcosis, with a corresponding change in electroencephalographic pattern and a lessening of the amount of thiopental administered. However, if a drug is given that produces apparently deeper narcosis without affecting the cortical electroencephalogram, the servomechanism will not be sensitive to this change and will continue to administer thiopental in terms of the requirements established by the findings on cortical electroencephalogram. In view of the work of Magoun [7] and others on the importance of the ascending reticular system in anesthesia, the need for electroencephalographic recording from areas other than the cortex is submitted for consideration.

The servomechanism is a feedback loop that attempts to reach equilibrium by meeting those changes in the patient's condition that it is able to detect. Systems have been constructed to measure and record all of the modalities observed by the anesthesiologist. Given a sufficiently complex computer that is able to interpret the meaning of these findings, the maintenance of an adequate level of clinical anesthesia by a multichannel servomechanism is not impossible. However, the number and type of observations and interpretations that such a machine can make will be limited by its construction. In a situation that calls for new powers of observation or interpretation, the servomechanism would be inadequate. It is this last limitation that probably explains the apparent discrepancy in our finding of altered operating conditions without a change being apparent in the cortical electroencephalogram.

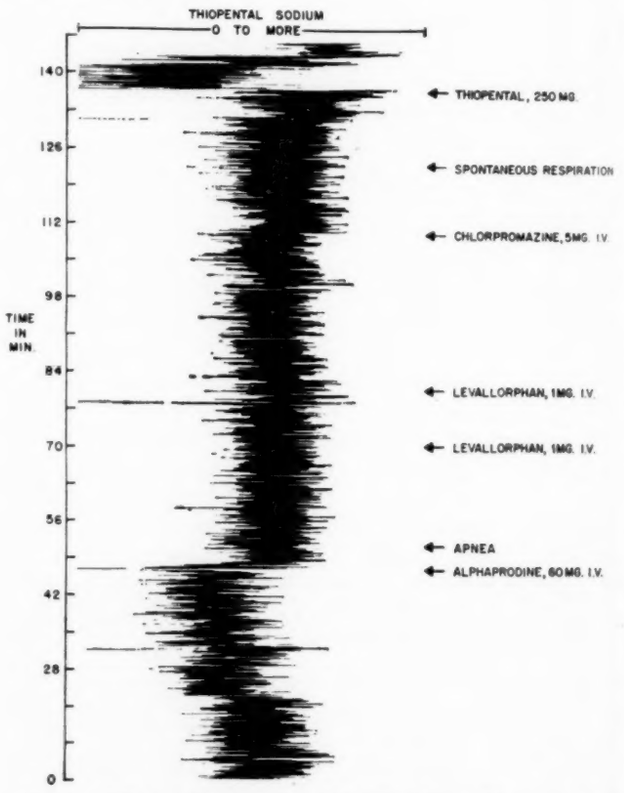


Fig. 3.—Effect of alphaprodine, levallorphan, chlorpromazine, and additional thiopental on rate of administration of thiopental regulated by servomotor. First three drugs do not alter rate of administration of thiopental, despite changes in clinical condition of patient. Administration of additional thiopental, however, depresses cortical electroencephalogram and, thereby, decreases amount of thiopental given by servomechanism.

That the requirement for thiopental during surgery can be reduced by the additional administration of alphaprodine is clear, for, in the series of Foldes and associates [8] of 852 patients, satisfactory operating conditions were obtained in 92 patients with the administration of alphaprodine and levallorphan alone, without thiopental.

## Conclusions

The administration of alphaprodine, levallorphan, and chlorpromazine does not alter the electroencephalographic response during light thiopental narcosis, nor does it decrease the dosage of thiopental required to maintain a constant electroencephalographic pattern showing light narcosis. The administration of alphaprodine and possibly chlorpromazine does produce clinical changes that result in more satisfactory operating conditions and, thereby, decreases the thiopental requirement by mechanisms that are not yet elucidated.

525 E. 68th St. (21) (Dr. Mazzia).

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# HOSPITAL HOUSE STAFFS, 1950-1955

**Harold S. Diehl, M.D., Minneapolis, Edwin L. Crosby, M.D., Chicago**
**and**
**Paul K. Kaetzel, A.B., Washington, D. C.**

*• More than three-fifths of the physicians who complete internships today continue specialty training without interruption. The number of internships and residencies offered in approved programs is nearly three times what it was before World War II. For 1955-1956, 8,780 interns and 21,213 residents were reported in training in the hospitals studied. Of the 8,780 interns, 2,300 were aliens. Analysis of the figures showed that the number of native interns had increased during the period studied but that the number of alien interns had increased much faster. Even so, 17% of the internships as well as 19% of the residencies were unfilled. The increase in the number of physicians taking specialty training since 1952 has been accounted for entirely by aliens. There has been a decrease in the number of residents specializing in tuberculosis and a striking increase in the number specializing in anesthesiology. The facts obtained by the Health Resources Advisory Committee afford a basis for consideration of many problems of the staffing of hospitals and the mobilization of medical resources.*

One of the significant developments in the training of physicians has been the expansion of hospital residency programs. Today, more than three-fifths of the physicians who complete internships continue specialty training without interruption. Others, upon discharge from military service, return to hospitals to begin or complete residencies.

Through these programs for graduate medical education, physicians have an opportunity to acquire and develop specialized knowledge and skills in diagnosis and treatment before entering medical practice. Incidental to this training, such physicians provide hospitals with needed staff and make significant contributions to the provision of medical care.

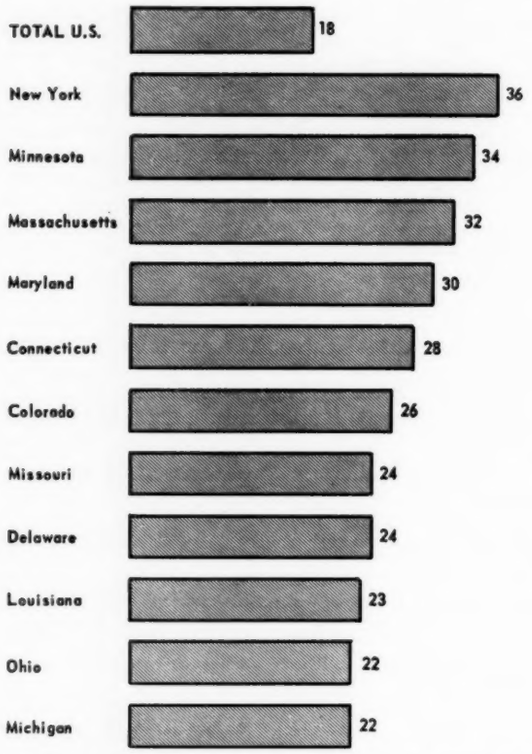
In recent years the demand for hospital services has increased tremendously. Between 1950 and 1955 hospital admissions rose from about 18 million to 21 million and the average daily hospital census increased from 1,250,000 to almost 1,400,000. Increase of population (due primarily to increases in both birth rates and longevity), a rising economic level, development of prepayment plans, and increasing awareness of health needs and medical advances have all contributed to the increased demand.

In 1955-1956, more than 38,000 internships and residencies were offered in approved programs at 1,400 hospitals. This compares to 30,000 positions offered by

Member, Health Resources Advisory Committee, and Dean of Medical Sciences, University of Minnesota (Dr. Diehl); Member, Health Resources Advisory Committee, and Executive Director, American Hospital Association (Dr. Crosby); and Member, Health Resources Advisory Committee Staff, Office of Defense Mobilization (Mr. Kaetzel).

1,100 hospitals in 1950 and only 13,000 prior to World War II. As shown in table 1, a considerable number of these positions have not been filled, although the percentage unfilled has been decreasing over the past three years. In 1950, 32% of the internships and 25% of the residencies were unfilled. The comparable figures for 1955 were 17 and 19% respectively.

The Korean war created an immediate and urgent need for additional medical and dental officers for the armed forces. In order to provide them, Congress




States with highest ratios of hospital house staffs per 100,000 civilian population, 1955.

passed Public Law 779, the "doctor-draft" act. Among other provisions, this law specified the order of call, by designating four different priority groups. Priorities 1 and 2 consisted of physicians and dentists who were permitted to continue their education during World War II; priority 3 included those who had neither deferment nor military service; and priority 4 consisted of veterans.

Since 1950, when the "doctor-draft" law become effective, the Health Resources Advisory Committee of the Office of Defense Mobilization has conducted yearly surveys of interns and residents in approved programs at hospitals. (The Health Resources Advisory Committee also serves as the National Advisory Committee to the Selective Service System.) Hospitals operated by the Department of Defense and the Public Health Service were excluded from these surveys. The purpose of these surveys has been to show (1) normal or existing staffing levels which could be used as "bench marks" in mobilization planning and (2) the extent of losses due to military withdrawals under the "doctor-draft" law. Participation by hospitals having approved training programs was 97% or higher in each of the six survey years.

TABLE 1.—*Total Number of U. S. Hospitals with A. M. A. Approvals for Internship and Residency Programs: Number of Available Positions and Percentage Unfilled Each Year, 1950-1955**

| Year | Internships | | | Residencies | | |
|---|---|---|---|---|---|---|
| | No. Hospitals | No. Positions | % Unfilled | No. Hospitals | No. Positions | % Unfilled |
| 1950-1951 | 828 | 10,044 | 32 | 1,120 | 19,364 | 25 |
| 1951-1952 | 865 | 11,467 | 28 | 1,123 | 20,645 | 23 |
| 1952-1953 | 853 | 11,006 | 28 | 1,131 | 22,292 | 24 |
| 1953-1954 | 844 | 10,624 | 22 | 1,154 | 23,628 | 21 |
| 1954-1955 | 850 | 11,048 | 18 | 1,181 | 25,486 | 20 |
| 1955-1956 | 867 | 11,616 | 17 | 1,202 | 26,516 | 19 |

* Data from Annual Report on Internships and Residencies, J. A. M. A., Sept. 29, 1951; Sept. 27, 1952; Sept. 26, 1953; Sept. 25, 1954; Sept. 24, 1955; and Sept. 22, 1956.

## House Staffs, 1955-1956

For 1955-1956, 8,780 interns and 21,213 residents were reported in training at hospitals in 45 states, the District of Columbia, the Canal Zone, Hawaii, and Puerto Rico. (Here and elsewhere in this report, the term "residents" includes second-year and third-year interns, residents, and fellows. The term "interns" includes only first-year interns.) Over one-half of these interns and residents were in six states—New York, Pennsylvania, California, Ohio, Illinois, and Massachusetts. New York and Massachusetts ranked first and third, respectively, in number of house staff per 100,000 civilian population (see figure).

TABLE 2.—*Percentage of Change, Since 1950, in Number of Interns and Residents in Approved Programs at Hospitals**

| Training Year | Total House Staff | | Intern House Staff | | Resident House Staff | |
|---|---|---|---|---|---|---|
| | No. | % Change from 1950-1951 | No. | % Change from 1950-1951 | No. | % Change from 1950-1951 |
| 1950-1951 | 24,442 | | 6,237 | | 18,205 | |
| 1951-1952 | 22,918 | − 6.2 | 6,783 | + 8.8 | 16,135 | −11.4 |
| 1952-1953 | 23,221 | − 5.0 | 6,990 | +12.1 | 16,231 | −10.8 |
| 1953-1954 | 25,896 | + 5.9 | 7,705 | +23.5 | 18,191 | − 0.1 |
| 1954-1955 | 28,146 | +15.2 | 8,178 | +31.1 | 19,968 | + 9.7 |
| 1955-1956 | 29,993 | +22.7 | 8,780 | +40.8 | 21,213 | +16.5 |

* Excluding Department of Defense and Public Health Service Hospitals.

TABLE 3.—*Percentage of Change, Since 1950, in Number of Citizen and Alien Interns and Residents in Approved Programs at Hospitals**

| Training Year | Total House Staff | | Intern House Staff | | | | Resident House Staff | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % Change from 1950-1951 | Citizens | % Change from 1950-1951 | Aliens | % Change from 1950-1951 | Citizens | % Change from 1950-1951 | Aliens | % Change from 1950-1951 |
| 1950-1951 | 24,442 | | 5,515 | | 722 | | 16,855 | | 1,350 | |
| 1951-1952 | 22,918 | − 6.2 | 5,667 | + 2.8 | 1,116 | + 54.6 | 13,902 | −17.5 | 2,233 | + 65.4 |
| 1952-1953 | 23,221 | − 5.0 | 5,637 | + 2.2 | 1,353 | + 87.4 | 13,196 | −21.7 | 3,035 | +124.8 |
| 1953-1954 | 25,896 | + 5.9 | 5,918 | + 7.3 | 1,787 | +147.5 | 14,389 | −14.6 | 3,802 | +181.6 |
| 1954-1955 | 28,146 | +15.2 | 6,187 | +12.2 | 1,991 | +175.8 | 15,264 | − 9.4 | 4,704 | +248.4 |
| 1955-1956 | 29,993 | +22.7 | 6,487 | +17.6 | 2,293 | +217.6 | 15,633 | − 7.3 | 5,580 | +313.3 |

* Excluding Department of Defense and Public Health Service hospitals.

Of physicians in training, 45% were in the 140 general hospitals with medical school teaching affiliations; 45% were in 1,100 other general hospitals; and 10% were in mental, tuberculosis, and other special hospitals.

house staffs numbered about 23,000, a level only 5% below the 1950 total. In each of the three subsequent years (1953-1955), hospital house-staff totals showed an increase over the 1950 level—6% in 1953, 15% in 1954, and 23% in 1955 (table 2).

TABLE 4.—*Alien Physicians Training in A. M. A.-Approved Programs in Hospitals in U. S. and Territories, as Percentage of Total House Staffs, 1955-1956 Training Year**

| State and Territory | Total House Staff | | | Intern House Staff | | | Resident House Staff | | |
|---|---|---|---|---|---|---|---|---|---|
| | Total Staff | Alien Staff | % | Total Staff | Alien Staff | % | Total Staff | Alien Staff | % |
| Total | 29,993 | 7,873 | 26.2 | 8,780 | 2,293 | 26.1 | 21,213 | 5,580 | 26.3 |
| New England | 2,529 | 731 | 28.9 | 594 | 169 | 28.5 | 1,935 | 562 | 29.0 |
| Connecticut | 631 | 202 | 32.0 | 179 | 55 | 30.7 | 452 | 147 | 32.5 |
| Maine | 44 | 8 | 18.2 | 22 | 5 | 22.7 | 22 | 3 | 13.6 |
| Massachusetts | 1,624 | 460 | 28.3 | 336 | 102 | 30.4 | 1,288 | 358 | 27.8 |
| New Hampshire | 37 | 3 | 8.1 | 12 | ... | ... | 25 | 3 | 12.0 |
| Rhode Island | 126 | 44 | 34.9 | 34 | 7 | 20.6 | 92 | 37 | 40.2 |
| Vermont | 67 | 14 | 20.9 | 11 | ... | ... | 56 | 14 | 25.0 |
| Central Atlantic | 10,203 | 3,495 | 34.3 | 2,877 | 970 | 33.7 | 7,326 | 2,525 | 34.5 |
| Delaware | 93 | 24 | 25.8 | 25 | 2 | 8.0 | 68 | 22 | 32.4 |
| District of Columbia | 541 | 170 | 31.4 | 142 | 42 | 29.6 | 399 | 128 | 32.1 |
| Maryland | 809 | 293 | 36.2 | 216 | 65 | 30.1 | 593 | 228 | 38.4 |
| New Jersey | 769 | 523 | 68.0 | 373 | 283 | 75.9 | 396 | 240 | 60.6 |
| New York | 5,770 | 2,005 | 34.7 | 1,460 | 526 | 36.0 | 4,310 | 1,479 | 34.3 |
| Pennsylvania | 2,097 | 405 | 19.3 | 608 | 18 | 3.0 | 1,489 | 387 | 26.0 |
| West Virginia | 124 | 75 | 60.5 | 53 | 34 | 64.2 | 71 | 41 | 57.7 |
| South East | 3,528 | 490 | 13.9 | 1,105 | 162 | 14.7 | 2,423 | 328 | 13.5 |
| Alabama | 224 | 14 | 6.3 | 75 | 5 | 6.7 | 149 | 9 | 6.0 |
| Arkansas | 108 | 9 | 8.3 | 38 | 2 | 5.3 | 70 | 7 | 10.0 |
| Florida | 314 | 76 | 24.2 | 116 | 31 | 26.7 | 198 | 45 | 22.7 |
| Georgia | 408 | 52 | 12.7 | 115 | 16 | 13.9 | 293 | 36 | 12.3 |
| Kentucky | 256 | 76 | 29.7 | 73 | 32 | 43.8 | 183 | 44 | 24.0 |
| Louisiana | 680 | 27 | 4.0 | 218 | 20 | 9.2 | 462 | 7 | 1.5 |
| Mississippi | 10 | 1 | 10.0 | 3 | ... | ... | 7 | 1 | 14.3 |
| North Carolina | 403 | 44 | 10.9 | 105 | 4 | 3.8 | 298 | 40 | 13.4 |
| South Carolina | 135 | 8 | 5.9 | 68 | 1 | 1.5 | 67 | 7 | 10.4 |
| Tennessee | 537 | 93 | 17.3 | 156 | 27 | 17.3 | 381 | 66 | 17.3 |
| Virginia | 453 | 90 | 19.9 | 138 | 24 | 17.4 | 315 | 66 | 21.0 |
| South West | 1,184 | 251 | 21.2 | 387 | 61 | 15.8 | 797 | 190 | 23.8 |
| Arizona | 89 | 44 | 49.4 | 53 | 24 | 45.3 | 36 | 20 | 55.6 |
| New Mexico | 18 | ... | ... | ... | ... | ... | 18 | ... | ... |
| Oklahoma | 188 | 19 | 10.1 | 68 | 7 | 10.3 | 120 | 12 | 10.0 |
| Texas | 889 | 188 | 21.1 | 266 | 30 | 11.3 | 623 | 158 | 25.4 |
| East North Central | 6,200 | 1,771 | 28.6 | 1,986 | 572 | 28.8 | 4,214 | 1,199 | 28.5 |
| Illinois | 1,915 | 710 | 37.1 | 678 | 282 | 41.6 | 1,237 | 428 | 34.6 |
| Indiana | 316 | 14 | 4.4 | 93 | 1 | 1.1 | 223 | 13 | 5.8 |
| Michigan | 1,557 | 293 | 18.8 | 432 | 53 | 12.3 | 1,125 | 240 | 21.3 |
| Ohio | 1,957 | 682 | 34.8 | 630 | 197 | 31.3 | 1,327 | 485 | 36.5 |
| Wisconsin | 455 | 72 | 15.8 | 153 | 39 | 25.5 | 302 | 33 | 10.9 |
| West North Central | 2,812 | 672 | 23.9 | 672 | 184 | 27.4 | 2,140 | 488 | 22.8 |
| Iowa | 277 | 54 | 19.5 | 63 | 14 | 22.2 | 214 | 40 | 18.7 |
| Kansas | 304 | 59 | 19.4 | 66 | 10 | 15.2 | 238 | 49 | 20.6 |
| Minnesota | 1,079 | 215 | 19.9 | 183 | 36 | 19.7 | 896 | 179 | 20.0 |
| Missouri | 1,004 | 315 | 31.4 | 298 | 102 | 34.2 | 706 | 213 | 30.2 |
| Nebraska | 110 | 7 | 6.4 | 32 | 2 | 6.3 | 78 | 5 | 6.4 |
| North Dakota | 19 | 9 | 47.4 | 15 | 7 | 46.7 | 4 | 2 | 50.0 |
| South Dakota | 19 | 13 | 68.4 | 15 | 13 | 86.7 | 4 | ... | ... |
| Rocky Mountain | 557 | 104 | 18.7 | 161 | 30 | 18.6 | 396 | 74 | 18.7 |
| Colorado | 395 | 72 | 18.2 | 108 | 16 | 14.8 | 287 | 56 | 19.5 |
| Montana | 9 | 9 | 100.0 | 4 | 4 | 100.0 | 5 | 5 | 100.0 |
| Utah | 153 | 23 | 15.0 | 49 | 10 | 20.4 | 104 | 13 | 12.5 |
| Far West | 2,748 | 305 | 11.1 | 883 | 127 | 14.4 | 1,865 | 178 | 9.5 |
| California | 2,265 | 233 | 10.3 | 699 | 98 | 14.0 | 1,566 | 135 | 8.6 |
| Oregon | 213 | 26 | 12.2 | 64 | 11 | 17.2 | 149 | 15 | 10.1 |
| Washington | 270 | 46 | 17.0 | 120 | 18 | 15.0 | 150 | 28 | 18.7 |
| Territories | 232 | 54 | 23.3 | 115 | 18 | 15.7 | 117 | 36 | 30.8 |
| Canal Zone | 35 | 6 | 17.1 | 18 | 1 | 5.6 | 17 | 5 | 29.4 |
| Hawaii | 73 | 42 | 57.5 | 28 | 16 | 57.1 | 45 | 26 | 57.8 |
| Puerto Rico | 124 | 6 | 4.8 | 69 | 1 | 1.4 | 55 | 5 | 9.1 |

* Excluding Department of Defense and Public Health Service hospitals.

## Five-Year Trends

*Total Number of Interns and Residents.*—In 1950, before the mobilization of physicians got under way, hospitals had staffs of more than 24,000 interns and residents. In 1951 and in 1952, in spite of extensive withdrawals under the "doctor-draft" law, hospital

Over the five-year period, there was an annual increase in the number of interns, with the 1955 total 40% above the 1950 figure. On the other hand, the number of residents in 1951 and 1952 was about 2,000 less than in 1950. In 1953, the number of residents approximated the 1950 total; in 1954, there were 10% more; and in 1955, 17% more than in 1950.

These increases are reflections of increases both in numbers of medical school graduates and in numbers of alien physicians taking training in this country. In addition, for the past several years, the armed forces have been returning physicians to civilian life at about the same rate as they have been withdrawing from it.

*Citizenship Status.*—As pointed out earlier, comparison of 1955-1956 data with those of 1950-1951 shows an over-all increase of 23% in house-staff members. When the data for citizens and aliens are viewed separately, a somewhat different picture appears (table 3). Over the five-year period the citizen group showed a slight (1%) decrease—22,120 as compared to 22,370—while the alien group increased 280%, from 2,072 to 7,873.

Over this five-year period the total number of interns increased from 6,237 to 8,780, or 40%. The citizen portion of the increase, however, was only about 1,000, or 18%, while the alien portion increased from 700 to 2,300, or 218%. The total number of residents increased from 18,205 to 21,213, or 16% since 1950, with all of the increase accounted for by the alien group, which increased more than 300%. In fact, between 1950 and 1952, the number of citizens taking residencies dropped from 16,855 to 13,196—a 22% decrease. This was due to military withdrawals from the age group which normally fills residencies. In 1953, numbers of citizen residents in training began to increase, and, by 1955, although the number was 7% below the 1950 level, it was 18% above the five-year low in 1952.

TABLE 5.—*Percentage of Change, Since 1950, in Number of Residents in Approved Positions at Hospitals, by Specialty**

| Specialty | No. of Physicians 1950-1951 | No. of Physicians 1955-1956 | % Change from 1950-1951 |
|---|---|---|---|
| Total | 18,205 | 21,213 | +16.5 |
| General practice | 416 | 531 | +27.6 |
| Eye, ear, nose, and throat | 790 | 784 | — 0.8 |
| Internal medicine | 4,268 | 4,436 | + 3.9 |
| Obstetrics and gynecology | 1,641 | 1,934 | +17.9 |
| Pathology | 794 | 1,077 | +35.6 |
| Pediatrics | 1,105 | 1,290 | +16.7 |
| Neurology and/or psychiatry | 1,746 | 2,332 | +34.0 |
| Radiology | 870 | 1,108 | +27.4 |
| Tuberculosis | 298 | 225 | —24.5 |
| General surgery | 4,406 | 4,955 | +12.5 |
| Anesthesiology | 509 | 845 | +66.0 |
| Orthopedic surgery | 633 | 719 | +13.6 |
| Urology | 352 | 423 | +20.2 |
| Other | 383 | 554 | +44.6 |

* Excluding Department of Defense and Public Health Service Hospitals.

By 1955, more than 900 of the 1,400 hospitals with approved graduate medical education programs had one or more aliens in training, with about one-half of the aliens concentrated in four states—New York, Illinois, Ohio, and New Jersey. States which reported high proportions of alien house staffs were New Jersey, 68.0%; West Virginia, 60.5%; Arizona, 49.4%; Illinois, 37.1%; Maryland, 36.2%; Rhode Island, 34.9%; Ohio 34.8%; and New York, 34.7% (table 4).

*Priority Distribution.*—The "doctor-draft" law specified the order of call to military service of medical and dental personnel by designating four priority groups. The proportion of house-staff members reported in priorities 1 and 2 decreased from 24% in 1950 to an almost negligible number in 1955.

The number of priority 3 physicians in training increased from about 3,000 in 1950 to about 4,200 in 1955. This is a reflection of the rising proportion of nonveteran graduates who have been deferred for the completion of their education and an internship. Priority 3 registrants comprised 18% of the interns and 10% of the residents in 1950, as compared to 32% of the interns and 7% of the residents in 1955.

House staffs in 1950 through 1953 were made up increasingly of priority 4 physicians. These men were veterans of World War II or Korea. By 1953, priority 4 physicians accounted for more than one-half of all physicians in training. Beginning with 1954, the proportion of house-staff members who were priority 4 dropped, and, by 1955, although there were about 2,000 more in training than in 1950, they comprised about the same proportion of total staff—40%.

*Hospital Specialty Service.*—Despite the over-all increase of 16% in the number of residents between 1950 and 1955, there was a decrease of 24% in the number of residents specializing in tuberculosis. The number on eye, ear, nose, and throat services showed no change during this five-year period. Increases occurred in all of the other specialties, the largest being a 66% increase in anesthesiology. Other substantial increases were pathology, 36%; neurology and psychiatry, 34%; general practice, 28%; and radiology, 27% (table 5). Internal medicine, which accounted for 21% of the total residents in 1955, and general surgery, which accounted for 23%, increased 4 and 12%, respectively, between 1950 to 1955.

## Future Outlook

An increase in the number of citizen interns is anticipated for the years immediately ahead. Medical school enrollments are at record levels. Since 1951, two new schools have gone into operation and are now graduating students. Another school began enrolling students in 1955 and will graduate the first class in 1959. Two other schools, which formerly had two-year programs, are in the process of developing four-year programs and will graduate students by 1957.

Since 1952, the increase in the number of physicians taking specialty training has been accounted for entirely by aliens. The next few years, however, should bring an increase in the number of citizen residents. Even if the proportion of each graduating class that takes residency training remains constant, the increase in the number of medical school graduates will result in an increase in the number of citizens taking residency training.

## Summary and Conclusions

Hospital house-staff surveys have been conducted annually, since 1950, by the Health Resources Advisory Committee of the Office of Defense Mobilization. Some of the important aspects of the analysis of these surveys are as follows: 1. Over the five-year period the total number of interns in approved programs in hospitals has increased by 40.8% and the number of

residents by 16.5%. 2. The number of interns who are United States citizens increased by 1,000, or 18%, and the number who are noncitizens by 1,600, or 218%. 3. In 1955, the number of residents who were citizens was 7% below the 1950 level. There was a decrease of 22% between 1950 and 1952 as a result of withdrawals to enter military service during the Korean war, but since that time the number has been increasing. The number of noncitizen residents increased by 4,200, or more than 300%, during the five-year period. 4. About one-half of the noncitizens were concentrated in four states—New York, Illinois, Ohio, and New Jersey. 5. The proportion of house-staff members reported in priorities 1 and 2, as designated under the "doctor-draft" act, decreased from 24% in 1950 to an almost negligible number in 1955; priority 3 registrants comprised 18% of the interns and 10% of the residents in 1950, as compared to 32% of the interns and 7% of the residents in 1955; and priority 4 registrants accounted for about the same percentage in 1955 as in 1950—40%. 6. During the five-year period there was a decrease of 24% in the number of residents specializing in tuberculosis. With the exception of eye, ear, nose, and throat, which showed no change, increases occurred in all of the other specialties, the largest being a 66% increase in anesthesiology.

These annual tabulations of hospital house staffs have provided the Health Resources Advisory Committee with data necessary for the successful execution of its responsibilities and provide a potential basis for adjustment of staffing in case of more active mobilization.

40 Barton Ave. S. E. (14) (Dr. Diehl).

# CLINICAL NOTES

## BEDSIDE DETERMINATION OF UREA NITROGEN LEVEL IN SERUM OR PLASMA

**Elma C. Lile, A.B., Mario F. Villamil, M.D., Mark C. Rhees, M.S.**
**and**
**Belding H. Scribner, M.D., Seattle**

A quick, accurate test for determining the serum urea nitrogen level is needed for night and emergency work and for routine office screening. Caraway [1] describes a rapid turbidity method for determination of urea nitrogen level with use of xanthydrol. We find his method to be only semiquantitive; it is able to determine whether the urea nitrogen level is normal or above normal but does not measure satisfactorily the degree of elevation. Also, the timing is extremely critical. The urea nitrogen test described here is performed on a drop of serum or plasma and is accurate enough for routine clinical needs over the range of 4 to 300 mg. per 100 cc. It uses a minimum of equipment and stable reagents and is a simple, two-minute test.

### Principle of Method

The method proposed here is a modification of the method of Van Slyke and Cope.[2] One drop of glycerin (glycerol) urease extract (Harleco) is added directly to one drop of serum to hydrolyze the urea to ammonia. The hydrolysis is complete within one minute at room temperature. The mixture is then diluted with isotonic sodium chloride solution and Nessler's reagent is added to produce color. The depth of this color, and hence the urea nitrogen concentration, is determined by comparison with color standards made by Nesslerizing solutions of ammonium sulfate. A set of permanent color standards can also be used in the 0-30 mg. per 100 cc. range, and this makes the procedure a little faster when it is used as a screening test. It should be noted that the color is developed in the presence of plasma proteins, which eliminates the necessity for preparing a protein-free filtrate.

From the Veterans Administration Hospital and the Department of Medicine, University of Washington School of Medicine.

### Equipment

The equipment includes (1) two bottles—one 2-oz. plastic bottle for Nessler's reagent and one ½-oz. bottle for glycerin urease solution; (2) three droppers—one to deliver the sample (select a standard medicine dropper with an average-size tip; if in doubt check delivery, which, when the dropper is held vertically, should be about 0.4 cc. per 10 drops), one for the urease bottle, and one for the Nessler's reagent that delivers 0.7 to 1.0 cc. per delivery; (3) four test tubes—Pyrex culture tubes 13 by 100 mm. (Corning 9820) to be calibrated by scratching a mark at 3 cc.; (4) a standard 1-cc. tuberculin syringe for measuring the standard ammonium sulfate solution (measurement is facilitated if the barrel of a 20-gauge hypodermic needle is cut away from its hub, filed to reopen the lumen, and cemented into the tip of the syringe); and (5) permanent color standards. Permanent color standards are not essential but can be used for determinations under 30 mg. per 100 cc. and have colors representing urea nitrogen concentration of 10, 20, and 30 mg. per 100 cc. The following two solutions are required to make up these three color standards: an aqueous solution of phenolsulfonphthalein containing 40 mg. of the water-soluble sodium salt in 1,000 cc. and any buffer solution of pH 5.0 ± 0.2. (Use Coleman blue label certified buffer tablets or make according to instructions in standard textbooks.)

The individual color standards are made up by using the proportions of the above reagents given in the table. The color standards should be sealed in

ampuls made from 13 by 100 mm. Pyrex culture tubes. If the ampuls are boiled for one-half hour after sealing, the colors will remain stable indefinitely.

This equipment can be conveniently combined into a small portable kit or included in a larger kit that contains bedside tests for chloride,[3] bicarbonate,[4] and sodium.[5]

## Reagents

The four reagents used are as follows:

1. Glycerin urease extract. This appears to be stable indefinitely at room temperature. However, it is recommended that the stock bottle be stored in the refrigerator and the supply in the kit be renewed every four to six months.

2. Nessler's reagent.[6] For Nessler's reagent add 45.5 Gm. of mercuric iodide and 34.9 Gm. of potassium iodide to a 1-liter volumetric flask and dissolve in 500 cc. of distilled water. Add slowly to this mixture 200 cc. of 10 *N* potassium hydroxide (or an equivalent amount of another concentration). Dilute to 1 liter. Protect this reagent from atmospheric carbon dioxide. If the reagent is clear, it can be used immediately. If there is any turbidity, this can be reduced by storing the reagent in the dark for about two months. A small supply of Nessler's reagent is kept in a plastic bottle in the kit. Keep the dropper out of the bottle in the kit or the rubber bulb will react with the reagent.

*Preparation of Color Standards by Placing Indicated Amount of Phenolsulfonphthalein in 100-Cc. Volumetric Flask and Diluting to 100 Cc. with Buffer*

| Standard, Mg./100 Cc. | Phenolsulfonphthalein, Cc. | pH 5.0 Buffer, Cc. |
|---|---|---|
| 10 | 7.7 | 92.3 |
| 20 | 12.5 | 87.5 |
| 30 | 22.7 | 77.3 |

3. Standard ammonium sulfate solution. This contains 188.6 mg. of ammonium sulfate per liter of approximately 0.1 *N* sulfuric acid.

4. Isotonic solution of sodium chloride (9 Gm. per liter). This is used to dilute samples of serum or plasma and is conveniently dispensed in a small plastic wash bottle.

## Procedure

The basic procedure is as follows (test tubes must be rinsed free of Nessler's reagent):

1. Measure 0.04 cc. (1 drop) of serum or plasma into one of the 13 by 100 mm. Pyrex culture tubes. This measurement can be accomplished in one of two ways: For most clinical needs measurement with a dropper is sufficiently accurate. Deliver one drop from the sample dropper described above, being sure that the drop strikes the bottom of the tube. If the drop runs down the sides a low result will be obtained. The second method is to use an appropriate volume of any convenient dilution of serum in isotonic sodium chloride solution; for example, 1 cc. of a 1:25 dilution. It is convenient to use a tuberculin syringe to measure the sample and make the dilution in a graduated centrifuge tube.

2. Add 1 drop of glycerin urease extract.

3. Shake or tap the tube so that all of the sample is completely mixed with the glycerin urease.

4. Wait one minute.

5. If permanent color standards are not available, prepare color standards in the expected range as follows: Place 0.04 cc. or 1 drop of serum in each of the 13 by 100 mm. Pyrex tubes to be used as a color standard. (In addition to the ammonium sulfate, each standard tube contains approximately the same amount of serum as the unknown tube. This is essential, since the protein modifies the final color developed when Nessler's reagent is added.) Add the appropriate ammonium sulfate with the tuberculin syringe. Each 0.01-cc. division on the syringe equals 1 mg. per 100 cc. Thus, to make a 20 mg. per 100 cc. standard, 0.2 cc. of ammonium sulfate would be added to the tube.

6. Dilute unknown and standard tubes to the 3-cc. mark with isotonic sodium chloride solution.

7. Add 1 dropperful of Nessler's reagent (0.7-1.0 cc.) to each tube. Since the color depends to some extent on the technique of adding the Nessler's reagent, the following standardized technique of addition is recommended: Fill the dropper by means of a complete compression of the dropper bulb so that a relatively constant amount of reagent will be delivered. Point the tip down the side of the 13 by 100 mm. tube and deliver all the Nessler's reagent with one strong squirt that effects instant and complete mixing without producing bubbles.

8. If the sample remains clear upon addition of Nessler's reagent, compare with the color standards to determine the concentration of urea nitrogen. If the sample clouds, proceed immediately to the technique for high urea nitrogen levels (see below). If the sample color falls outside the range of the color standards, repeat the entire procedure, making up standards in the appropriate range. Also remake the sample, as it will darken on standing more than a few minutes. If a result of less than 10 mg. per 100 cc. is obtained, the test tube is probably contaminated with Nessler's reagent from the previous test and this has inactivated the urease.

Following is the technique for high urea nitrogen levels:

1. The sample size for this technique is 0.008 cc. of serum or plasma. This can be measured in one of two ways, depending on convenience and the accuracy desired. The first method is to place 1 drop of serum measured with a dropper in a small test tube. Rinse the dropper and add 4 drops of isotonic sodium chloride solution mixed. One drop of this dilution will contain about 0.008 cc. of original sample. Since the color comparisons are quite accurate with elevated urea nitrogen levels, sample measurement with a dropper introduces a significant error. Hence, if greater than ± 15% accuracy is desired, the second method of sample measurement should be used. For this, use an appropriate volume of any convenient dilution of serum in isotonic sodium chloride solution. For example, if a 1:25 dilution was previously prepared for the first part of the test, 0.2 cc. of this could be used, which is equivalent to 0.008 cc. of original sample.

2. Measure the equivalent of 0.008 cc. of original sample in each of 4 Pyrex test tubes (13 by 100 mm.) that have been calibrated to 3 cc.

3. Add 1 drop of glycerin urease to one of the four test tubes. This becomes the unknown. Wait one minute.

4. Using the tuberculin syringe, add ammonium sulfate solution to each of the other test tubes to make standards in the range expected. Usually one would make a 100, 150, and 200 mg. per 100 cc. standards. It requires 0.2 cc. of the standard ammonium sulfate for each 100 mg. per 100 cc.

5. Dilute with isotonic sodium chloride solution all four tubes to approximately the 3 cc. mark, though the final volume need not be exact.

6. Add 0.7 to 1.0 cc. of Nessler's reagent, using the technique described above. It is important that the same technique be used on all tubes.

7. Wait one minute for full color development, and then compare the unknown with the standards by looking lengthwise down through the four tubes toward a white surface.

8. Estimate the urea nitrogen level from this comparison.

9. If the unkown falls outside the range of the standards, repeat the entire procedure, making appropriate standards. Do not use the original unknown, as it may darken on standing more than a few minutes.

## Result

One hundred thirty samples were analyzed for urea nitrogen by the bedside method, and the results were compared with those obtained by the method of Van Slyke and Cope [2] with use of a Somogyi filtrate. In the range of 4 to 30 mg. per 100 cc. of urea nitrogen the standard deviation on 95 samples was ± 3.0 mg. per 100 cc., with a maximum deviation of 7.0 mg. In the critical range of 18 to 22 mg. per 100 cc. the standard deviation on 22 samples was ± 2.1 mg. per 100 cc., with a maximum deviation of 2.5 mg. In the range of 30 to 100 mg. per 100 cc. the standard deviation on 22 samples was ± 4.5 mg., with a maximum deviation of 9.0 mg.

The technique for high urea nitrogen levels, using accurately measured samples (rather than a dropper), gave the following results: The reproducibility on duplicate determination was at least ± 3%. When the results on 18 samples in the range of 100 to 300 mg. per 100 cc. were compared with those obtained by the method of Van Slyke and Cope [2] the standard deviation was ± 4.3 mg. per 100 cc. and the maximum deviation ± 15 mg.

## Sources of Error

*Turbidity.*—When the sample size is 0.04 cc. and the urea nitrogen concentration exceeds 100 mg. per 100 cc., turbidity will usually develop in both unknown and standard tubes. Since this can make comparisons inaccurate, all turbid specimens should be discarded and the test repeated with use of the 0.008-cc. sample size and the technique for high urea nitrogen levels. Nessler's reagent itself will become turbid on prolonged exposure to air; therefore, keep only a small supply in the kit. Renew the supply in the kit if turbidity develops.

*Contamination.*—Test tubes should be rinsed thoroughly with water after each determination. If any Nessler's reagent remains in the test tube, the mercury in the Nessler's reagent will inactivate the urease and no color will develop with the addition of Nessler's reagent.

*Jaundice and Hemolysis.*—Moderate to severe icterus and severe hemolysis make color comparison with the permanent color standards difficult and uncertain. However, since ammonium sulfate color standards made up with the icteric serum also contain the interfering color, comparison is not a problem. With icteric or hemolyzed serums, therefore, it is best to always make up ammonium sulfate color standards.

*Urease Deterioration.*—Urease may deteriorate after prolonged storage at room temperature, forming ammonia-containing products. To test for deterioration, place 2 drops of urease in a 13 by 100 mm. test tube and dilute to 3 cc. Add Nessler's reagent. Deterioration is indicated by the appearance within 30 seconds of color approaching the depth of the 10 mg. per 100 cc. standard.

## Checking Permanent Color Standards

The accuracy of the permanent color standards may be checked by comparing them to ammonium sulfate color standards prepared as described above.

## Clinical Applications

The simplicity of this technique for accurate measurement of urea nitrogen should make it possible to perform the test as a routine screening procedure on all patients from whom blood is drawn. This test should also prove of value in the emergency evaluation of critically ill patients. The technique for high urea nitrogen levels has a remarkable degree of reproducibility for such a simple test. This makes it possible to detect small day-to-day changes in the degree of elevation of the urea nitrogen level in uremic patients. Such information is of particular value in the management of patients with acute uremia.

## Summary

A simple, two-minute quantitative test for the direct determination of urea nitrogen level on serum or plasma is accurate enough for routine clinical use over the entire range of concentrations encountered in patients.

4435 Beacon Ave. (8) (Dr. Scribner).

This study was supported in part by grants from Abbott Laboratories, the American Heart Association, and the Schweppe Foundation.

A complete test kit for this procedure, as well as separate items of equipment, including sets of permanent color standards, are manufactured by Rochester Products Co., Rochester, Minn.

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5. Scribner, B. H., and Wiegert, H. T.: Bedside Determination of Total Base in Serum, J. A. M. A. **155:**639-644 (June 12) 1954.

6. Vanselow, A. P.: Preparation of Nessler's Reagent, Ind. & Eng. Chem. Analyt. Ed. **12:**516, 1940.

# COUNCIL ON DRUGS

Formerly the Council on Pharmacy and Chemistry

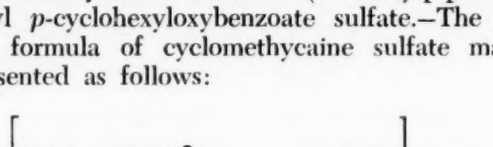
## NEW AND NONOFFICIAL DRUGS

Formerly New and Nonofficial Remedies

*Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Drugs are based on the evaluation of available scientific data and reports of investigations. Applicable commercial names for preparations of evaluated drugs are listed at the end of monographs and parenthetically in the text of supplemental statements; additional commercial names of which the Council is informed will be included with subsequently published supplemental statements and annual editions of New and Nonofficial Drugs.*

H. D. KAUTZ, M.D., *Secretary.*

**Cyclomethycaine Sulfate.**—3-(2-Methylpiperidino)-propyl *p*-cyclohexyloxybenzoate sulfate.—The structural formula of cyclomethycaine sulfate may be represented as follows:



*Actions and Uses.*—Cyclomethycaine sulfate, a topical anesthetic agent, belongs to the benzoic acid group of compounds, but its hydrolysis does not yield *p*-aminobenzoic acid. Hence, the anesthetic properties of the drug are not affected by concomitant sulfonamide therapy. Cyclomethycaine sulfate acts on damaged or diseased skin and on the mucosa of the rectum, vagina, urethra, and urinary bladder. The drug is relatively ineffective on the mucous membranes of the mouth, nose, trachea, bronchi, and eye. It does not penetrate the tympanic membrane and is, therefore, not beneficial in otitis media.

Cyclomethycaine sulfate is an effective topical anesthetic for abrasions and for certain types of surface skin lesions characterized by pain, pruritus, and cutaneous irritability. It also is useful for rectal and vaginal conditions in which pain arises in the mucous membrane or ulcerated fissures. After urethral instillation, the drug produces sufficient anesthesia to permit passage of sounds and cystoscopic examination. Cyclomethycaine has also been used for the relief of pain in burns. However, some experts in this field do not favor the use of topical anesthetics in burns, especially when large areas of the skin are involved, because of the increased hazard of systemic absorption.

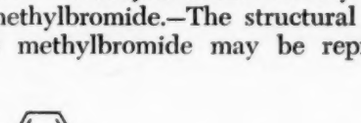
As with all topical anesthetic agents, cyclomethycaine sulfate carries a slight but predictable sensitizing potential when utilized on patients with allergies or in conditions of prolonged use. This fact should be borne in mind, especially when the drug is used in the rectum or vagina, although this potential is less than that with compounds comprising *p*-aminobenzoic acid; use of the drug should be discontinued immediately if manifestations of dermal or mucosal sensitivity occur.

*Dosage.*—Cyclomethycaine sulfate is applied topically as frequently as necessary to maintain surface anesthesia. For such use, the drug is administered in a suitable dermatological vehicle usually containing from 5 to 10 mg. per gram (0.5 to 1% concentration). For topical anesthesia of the rectum, 10 mg. of the drug may be administered, usually in the form of suppositories. For anesthesia of the urethra prior to urologic instrumentation, a jelly or solution containing 7.5 mg. per cubic centimeter (0.75% concentration) is used. The usual dose for intraurethral instillation is 2 to 10 cc. (15 to 75 mg.) in the male and 1 to 4 cc. (7.5 to 30 mg.) in the female.

Applicable commercial name: Surfacaine.

Eli Lilly and Company cooperated by furnishing scientific data to aid in the evaluation of cyclomethycaine sulfate.

**Pipenzolate Methylbromide.**—1-Ethyl-3-piperidyl benzilate methylbromide.—The structural formula of pipenzolate methylbromide may be represented as follows:



*Actions and Uses.*—Pipenzolate methylbromide, a synthetic anticholinergic agent with predominantly peripheral atropine-like effects, is closely related in chemical structure and pharmacological action to piperidolate hydrochloride. It is more potent than the latter agent, however, and produces a gastric antisecretory effect in addition to decreasing gastrointestinal motility. The drug appears to exert a more generalized spasmolysis than does piperidolate, since therapeutic doses usually affect the smooth musculature of the biliary tract also.

The chief clinical use of pipenzolate methylbromide is in the adjunctive treatment of peptic (gastric and duodenal) ulcer. It is no more effective than atropine in relieving hypermotility; however, it does decrease gastric secretion, thereby being somewhat more advantageous than atropine for this purpose. It should be borne in mind that anticholinergic therapy for peptic

ulcer should be adjunctive to proper dietary management. Pipenzolate also relaxes spasm of the lower gastrointestinal tract and the sphincter of Oddi and may therefore prove useful for the treatment of ileitis, the irritable colon syndrome, and other functional disorders of the gastrointestinal or biliary tracts.

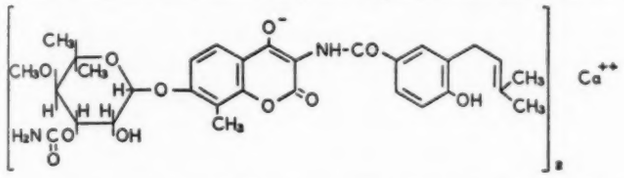
Side-effects associated with pipenzolate therapy are chiefly atropine-like in nature but, after therapeutic doses, are less severe and less frequent than with the belladonna alkaloids. No serious toxic reactions have been reported; however, the same precautions and contraindications should be observed with pipenzolate methylbromide as with other agents of this class.

*Dosage.*—Pipenzolate methylbromide is administered orally. The average dose for adults is 5 mg. three times daily before meals and 5 to 10 mg. at bedtime; however, dosage must be individualized to fit the needs and response of the particular patient.

Applicable commercial name: Piptal.

Lakeside Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of pipenzolate methylbromide.

**Novobiocin Calcium.**—The calcium salt of an antibiotic substance produced by fermentation from cultures of Streptomyces niveus.—The structural formula of novobiocin calcium may be represented as follows:

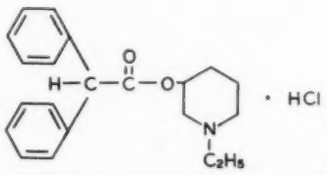


*Actions, Uses and Dosage.*—Novobiocin calcium has the same actions and uses as novobiocin sodium. It differs from the latter salt chiefly in being less alkaline and more stable in a liquid form. Accordingly, the calcium salt is primarily suited for oral administration in liquid form, especially for pediatric use or for those patients who prefer liquid medication to a solid form of the antibiotic. Novobiocin calcium is administered in the same dosage as the sodium salt. (See the monograph statement on novobiocin sodium in THE JOURNAL, Feb. 23, 1957, page 646.)

Applicable commercial name: Albamycin Calcium.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of novobiocin calcium.

**Piperidolate Hydrochloride.**—1-Ethyl-3-piperidyl diphenylacetate hydrochloride.—The structural formula of piperidolate hydrochloride may be represented as follows:



*Actions and Uses.*—Piperidolate hydrochloride, a synthetic derivative of a piperidol, antagonizes acetylcholine, chiefly at cholinergic nerve endings. Except in high doses, it does not block ganglions or inhibit transmission to skeletal muscle. Its effects on the central nervous system, on conduction within the heart, or on blood pressure, are minimal. The principal pharmacological actions of the drug are referable to inhibition of postganglionic parasympathetic nerve impulses. Thus, it may be classified as an anticholinergic agent with predominantly peripheral atropine-like effects. The clinical use of piperidolate hydrochloride is based on its ability to decrease motility of smooth muscle. There is evidence to indicate a high degree of specificity of the drug for the smooth muscle of the gastrointestinal tract; in therapeutic doses, it does not produce appreciable effects on the musculature of the biliary tract. Likewise, the drug has little, if any, effect on gastric secretion. After oral administration, demonstrable decreases in gastrointestinal motility are apparent within 10 to 20 minutes. This rapid action has been attributed to a local anesthetic effect.

Piperidolate hydrochloride has been used for the adjunctive management of functional gastrointestinal disorders characterized by pain, spasm, and hypermotility. The spasmolytic effect of the drug is more pronounced on the upper than on the lower portion of the gastrointestinal tract; thus it will inhibit gastroduodenal spasm, pylorospasm, and cardiospasm but is without appreciable effect on spasm of the colon. It has been demonstrated to relieve the spasm of the biliary sphincter and has been used clinically in various forms of biliary dyskinesia and other biliary disorders accompanied by spasm, as well as in various types of gastric neurosis and irritability.

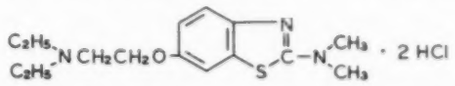
In therapeutic doses, piperidolate hydrochloride appears to be less toxic than atropine or other synthetic anticholinergic agents. It produces little xerostomia, dilation of the pupil, tachycardia, constipation, or other atropine-like side-effects. No urinary retention or increased intraocular pressure has so far been reported after its administration. Owing to its anticholinergic classification, however, the drug should be used with caution in patients with prostatic hypertrophy or glaucoma.

*Dosage.*—Piperidolate hydrochloride is administered orally. The dosage is governed by the severity of symptoms and the individual response. The average dose for adults is 50 mg. four times daily, preferably before meals and at bedtime.

Applicable commercial name: Dactil.

Lakeside Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of piperidolate hydrochloride.

**Diamthazole Dihydrochloride.**—6-(2-Diethylaminoethoxy)-2-dimethylaminobenzothiazole dihydrochloride.—The structural formula of diamthazole dihydrochloride may be represented as follows:



*Actions and Uses.*—Diamthazole dihydrochloride, an antifungal agent, is active in vivo against dermatophytes of the genera Trichophyton and Microsporum and against the monilial organism, Candida albicans. Its activity against bacteria and the common nonpathogenic molds is negligible. Although the precise mechanism of its antifungal action is imperfectly known, diamthazole has shown fungistatic properties in vitro; it also exerts a mild keratolytic effect and possesses antisporulating properties. The drug exhibits good diffusibility on the skin and, when applied in

moderate amounts to noninflamed dermal areas, is not absorbed to an appreciable extent into the systemic circulation.

Diamthazole dihydrochloride is used clinically for the treatment of superficial fungal infections caused by trichophytons, microsporums, and C. albicans. Repeated daily use has produced satisfactory results in chronic cases of tinea pedis (athlete's foot). Tinea capitis (ringworm of the scalp) caused by M. audouini or M. lanosum also responds to its use. The latter type of infection, however, often produces an inflammation or kerion and may react adversely to the drug if it is administered during this pyodermic phase. Cure rates for tinea capitis after use of diamthazole dihydrochloride range from 50 to 70%. Thus, the drug is not as effective as x-ray epilation, which can be expected to effect a cure rate of almost 100% when carried out by skilled personnel. The drug may be used in place of x-ray therapy in situations in which adequate facilities and personnel are not available or when total epilation is considered objectionable. Diamthazole may also be used for the treatment of tinea cruris, tinea corporis, and tinea versicolor. Dermatomycoses such as paronychia and onychomycosis caused by C. albicans have likewise been successfully treated with this agent. Since the drug is ineffective against bacteria, it may be necessary to administer suitable antibiotic agents along with diamthazole in order to combat concomitant or superimposed pyogenic infections of the skin.

In infants and very young children, ataxia, tremors, convulsions, hallucinations, and behavior changes have been reported after use of this drug, but there is more than a suggestion that these effects are due to sucking of fingers or of impregnated skull caps rather than to percutaneous absorption. Until more information can be accumulated, diamthazole dihydrochloride is nevertheless contraindicated in children under 2 years of age and should be used in reduced amounts in patients between the ages of 2 and 10. Also because of its possible neurotoxicity, the drug should not be used over extensive areas of the skin for the treatment of superficial fungus infections or tinea versicolor. Therapy should not be initiated during the acute or pyodermic phase of any fungus infection, and the drug should be applied on mucous membranes with caution. In adults, the only reported signs of toxicity are occasional local irritation and sensitization. In the event of these dermal manifestations or any systemic reaction, the use of the drug should be discontinued immediately.

*Dosage.*—Diamthazole dihydrochloride is administered topically to infected areas of skin. The drug is usually employed in 5% concentration in a suitable dermatological vehicle.

For tinea pedis, the acute or pyodermic phase of the infection should be pretreated with a 1:30 solution of aluminum acetate or a 1:10,000 potassium permanganate solution. Once the acute phase has subsided, the infected skin is treated once or twice daily with a 5% tincture of diamthazole dihydrochloride; a 5% ointment is applied at night. A 5% dusting powder may be sprinkled into shoes and stockings daily during treatment and afterwards to prevent recurrence.

For tinea capitis, hair should be clipped from the infected areas and the scalp washed frequently with a bland soap; the drug is then applied as a 5% tincture during the day, and a 5% ointment is rubbed into the infected areas before retiring. This daily regimen should be continued for at least three weeks after the first negative Wood's light examination. The drug should never be administered during the kerion phase of the infection.

For tinea versicolor, a 5% ointment is applied daily to the infected areas after a soap and water scrub. Although the infection is often more widespread than is clinically evident, the potential toxicity of the drug precludes its application to the entire body. A 5% dusting powder may be used to prevent recurrence or reinfection.

A 5% ointment or tincture of diamthazole dihydrochloride is applied twice a day to the involved areas for the treatment of tinea cruris, tinea corporis, paronychia, or onychomycosis.

Applicable commercial name: Asterol Dihydrochloride.

Hoffmann-La Roche Inc. cooperated by furnishing scientific data to aid in the evaluation of diamthazole dihydrochloride.

### Use of Sodium Acetrizoate for Urethrography

The Council has evaluated the usefulness and safety of sodium acetrizoate for retrograde urethrography. A preparation of the drug intended for this purpose (Thixokon) is rendered viscous by the addition of a relatively inert, nontoxic thickening agent. Nonviscous solutions of sodium acetrizoate (Urokon Sodium) have previously been described in N. N. R. as suitable for intravenous (excretory) urography, retrograde pyelography, intravenous nephrography and angiocardiography, translumbar arteriography, and intraductal cholangiography. On the basis of additional evidence, the Council concluded that the thickened solution of sodium acetrizoate is a useful contrast medium for the visualization of the lower urinary tract, including the urethra and its adnexa, the bladder neck, and under certain circumstances, the bladder mucosa. Except for occasional irritation to the urethra, the drug has not produced any serious side-effects or toxic reactions. It should nevertheless be administered with caution to patients with a definite history of allergy because of the possible occurrence of urethrovascular invasion.

For urethrography, 20 to 30 cc. of a 50% solution of the viscous material is introduced into the urethra by slow retrograde injection. Roentgenographic exposure is made at the end of the injection. If the patient has retained urine for two to three hours prior to examination, a satisfactory cystogram is obtained as well. After intraurethral injection of the drug, exposures made during micturition also provide adequate voiding urethrograms.

The Council voted to amend New and Nonofficial Drugs accordingly to describe this additional use of sodium acetrizoate.

Mallinckrodt Chemical Works cooperated by furnishing scientific data to aid in the evaluation of sodium acetrizoate for urethrography.

# COUNCIL ON FOODS AND NUTRITION

## Report to the Council

*The following paper was presented at the symposium, "The Relation of Proteins and Amino Acids to Human Nutrition," in Los Angeles, May 21, 1956. The symposium was sponsored by the Council on Foods and Nutrition, with the cooperation of the Los Angeles County Medical Society and the School of Medicine, University of California at Los Angeles. This report is the second of the series. After publication of the sixth and final report, this series will be available in monograph form.*

PHILIP L. WHITE, SC.D., *Secretary.*

# NITROGEN BALANCE AND THE NUTRITIVE VALUE OF PROTEINS

James B. Allison, Ph.D., New Brunswick, N. J.

Dietary proteins furnish the amino acids for synthesis of tissue proteins and for other special metabolic functions. Synthesis includes the rebuilding of tissue proteins that are being broken down continuously as well as the formation of the new proteins during growth. The process of synthesis is called anabolism; the process of breakdown, catabolism. For anabolism, the amino acids may be pictured as being activated and arranged in their proper places on the surface of an appropriate catalyst, there to be joined together through peptide linkages into a specific long polypeptide chain. This chain may then wind off the catalytic surface into a structure characteristic of the tissue protein formed by that catalyst.

### Dynamic State

Some tissue proteins are continuously being broken down and resynthesized, thereby creating a dynamic state in which nitrogen may flow from one tissue to another. This concept was revealed by the work of Whipple [1] and associates and given even more reality by recent experiments involving amino acids tagged with heavy nitrogen or radioisotopes.[2] Amino acids enter a dynamic metabolic pool contributed to by both dietary and tissue proteins, a pool to supply all of the amino acids needed for both catabolic and anabolic reactions.[3] This pool can be described as a summation of protein metabolism in many centers integrated into the dynamic state of the body as a whole. It is assumed that each center, at the cellular level, demands a properly balanced mixture of amino acids for anabolism, the amino acids being derived in part from extracellular sources.[4] The rate of turnover of different proteins, however, varies greatly; some being very labile, some less so, and some so stable that they draw from, but contribute little or nothing to, this metabolic pool. Such a dynamic state can result in the maintenance of one tissue at the expense of another.

The dynamic state of catabolism and anabolism in animals, in whom dietary and tissue amino acids are pictured as forming common metabolic pools, makes difficult the separation of the metabolism of amino acids from food (exogenous) from the metabolism of amino acids from tissues (endogenous). The concept of an endogenous metabolism, however, is valuable for recognizing certain metabolic pathways. Endogenous metabolism, for example, is often identified with the formation and excretion of creatinine, a substance essentially independent of amino acid intake, whereas exogenous metabolism is associated with the excretion of urea, which varies with the quantity and quality of dietary protein. The formation of creatinine, arising from special energy pathways involving creatine, can be correlated best with the functional nuclei of the muscle mass; the origin of urea can be associated with catabolism of amino acids of the metabolic pool. The excretion of creatinine can be increased by the addition of methionine and glycocyamine to the diet, another example of the ultimate effects that diet can exert upon most, if not all, body reactions.

### Essential Amino Acids

Twenty-two different amino acids ordinarily are required for synthesis of tissue proteins, and the absence of any one of them could prevent the formation of the polypeptide. The body can synthesize and mobilize the majority of these amino acids from dietary sources, but the classic studies of Rose [5] and his associates have demonstrated that some of the amino acids cannot be synthesized in amounts adequate for metabolic needs. These are called essential, the others nonessential. The essential amino acids must be provided *de novo* every day in the diet in proper amounts and proportions, together with an adequate supply of the nonessential amino acids or some nitrogen compound or compounds to provide the $NH_2$ groups needed for their synthesis, if protein synthesis and other metabolic functions are to take place normally. Examples of other functions are the formation of the hormones thyroxin or adrenalin from the amino acid tyrosine or the methylation of glycocyamine by amino acid methionine to form creatine, an essential compound in muscle metabolism.

The amount of nitrogen retained in the body is correlated, therefore, with the pattern of essential amino acids provided by the dietary protein. If that pattern is perfect for synthetic purposes, then the

From the Bureau of Biological Research, and the Department of Physiology and Biochemistry, Rutgers University.

dietary nitrogen fed, if not given in excess of synthetic needs, would be used in its entirety to build body protein. Such a pattern of essential amino acids is approached in egg white (table 1). The reference pattern of essential amino acids for growth in rats and dogs, listed in the first line of the table, was estimated from experiments on the requirements for growth and repletion of soft tissues in animals.

The reference pattern is calculated to simulate a dietary protein so that it can be compared with those of the food protein sources also listed in table 1. The pattern should not be taken as final but rather as a step toward determining a reference. It will vary from species to species and with the physiological state of the animal. Some of the essential amino acids recorded for dietary protein sources are in relative excess of values recommended in the reference pattern. Experimental data on the effects of amino acid imbalances indicate that, if the excesses are sufficiently great, the nutritive value would be reduced.[6] However, the data to be presented in this paper, together with information from the literature,[3] suggest that most of the nutritive values of natural protein sources are limited more by deficiencies in one or more of the essential amino acids than by excesses.

Nitrogen balance is, however, the algebraic sum of gains and losses of nitrogen in all the metabolic centers throughout the living system. It is possible for the body as a whole to be in positive balance and still lose nitrogen from some tissues. A striking example of this summation is the balance that develops in rats with a transplanted sarcoma in which the tumor-bearing body is in positive balance. The growing sarcoma, entering the dynamic state of the body, draws from, but contributes little to, the welfare of the tissues through a common metabolic pool. It is in positive balance; the liver also may be gaining in nitrogen, but the other soft tissues of the body are often losing labile protein stores.[6a]

These labile stores are the cytoplasmic proteins and the blood proteins, particularly plasma albumin, that rise or fall as the supply of amino acids increases or decreases in the diet. When these stores are filled maximally in the adult, catabolic activity is high, and the excretion of urea nitrogen derived from that activity is high. A relatively large amount of dietary nitrogen is needed to maintain these full stores. Expressed in terms of nitrogen balance, maintenance is established when the nitrogen intake just equals nitrogen excretion. Under these conditions nitrogen balance is zero, and the individual is said to be in nitrogen equilibrium. At equilibrium, the over-all catabolism of tissue nitrogen is equaled by anabolism. If, at any time, the amino acid intake, expressed as nitrogen, is not adequate to maintain these stores, they will be depleted through excess catabolism. Under these conditions nitrogen intake will be less than the nitrogen excretion so that nitrogen balance will be negative and the body will be losing nitrogen. Negative balance, therefore, means depletion in the labile protein stores. Continued feeding of a diet deficient in amino acids will cause a reduction in catabolic activity, as measured by excretion of urea nitrogen, and a reduction in the amount of nitrogen needed to maintain the individual in nitrogen equilibrium.

These labile protein stores provide a mechanism for the individual to adapt to various protein intakes. For example, a person with full stores who requires a high nitrogen intake for maintenance but who is placed on a lower nitrogen intake will go into negative balance, thereby losing body nitrogen. The resultant reduction in catabolism eventually brings about nitrogen equilibrium at the lowered intake. Conversely, an individual with reduced stores who is placed on a diet to produce positive balance will gain in body nitrogen. The increase in catabolic activity at the higher nitrogen intake will then produce equilibrium.

TABLE 1.—*Estimated Patterns of Amino Acids for Growth of Soft Tissues and for Maintenance of Nitrogen Equilibrium in Animals Compared with Patterns of Several Food Protein Sources**

| Pattern | Isoleucine | Leucine | Lysine | Methionine | Cystine | Phenylalanine | Threonine | Tryptophan | Valine |
|---|---|---|---|---|---|---|---|---|---|
| Reference for growth in rats and dogs | 4.2 | 5.6 | 5.0 | 5.0 | ... | 4.2 | 3.0 | 1.1 | 4.7 |
| Egg white | 6.4 | 8.8 | 7.2 | 4.2 | 3.2 | 5.9 | 4.9 | 1.2 | 7.5 |
| Egg powder | 9.0 | 6.2 | 6.1 | 3.2 | 2.3 | 5.6 | 4.9 | 1.1 | 7.0 |
| Beef | 5.2 | 7.8 | 8.6 | 2.7 | 1.5 | 3.9 | 4.4 | 1.0 | 5.1 |
| Casein | 6.3 | 10.0 | 8.1 | 3.2 | 0.4 | 5.4 | 4.5 | 1.0 | 7.4 |
| Peanut flour | 4.1 | 7.1 | 3.5 | 0.8 | 2.8 | 4.9 | 2.8 | 0.8 | 4.6 |
| Wheat gluten | 4.5 | 7.2 | 2.0 | 1.7 | 2.4 | 5.0 | 2.8 | 0.8 | 4.3 |

* From Allison.[3] All units in grams per 100 Gm. of protein.

If the food protein is deficient in one or more of the essential amino acids, tissue protein synthesis will be restricted, and some of the dietary amino acids will enter catabolic pathways, leading to the formation and excretion of nitrogen primarily in the form of urea. The pattern of amino acids illustrated by wheat gluten in table 1 is deficient in lysine and in tryptophan for maximum retention for synthetic purposes. For that reason, feeding wheat glutens increases the excretion of urinary nitrogen and results in a lower rate of synthesis of tissue proteins than that observed when egg proteins are included in the diet.

## Nitrogen Balance

The retention of nitrogen in the body is usually expressed as a nitrogen balance (B), which can be defined by the following equation in which I is dietary nitrogen intake, U is urinary nitrogen, and F is fecal nitrogen excreted: $B = I - (U + F)$. Neglecting the small loss of nitrogen through the skin in man, if nitrogen intake (I) is greater than the nitrogen excreted in the urine and feces (U + F), then the balance (B) is a positive figure and the body is gaining in nitrogen. A positive nitrogen balance means that the over-all anabolism of tissue nitrogen exceeds catabolism. Growing individuals would always be in positive balance. Similarly, adults should be in positive balance if they are in need of filling the protein stores.[7]

### Absorbed Nitrogen and Digestibility

The amount of nitrogen retained is accurately expressed as a function of the amount of dietary nitrogen absorbed into the body. Absorbed nitrogen (A) can be estimated according to the following equation in which I is dietary nitrogen intake, F is total fecal nitrogen, and $F_m$ is fecal nitrogen of body origin, $(F - F_m)$ thereby being fecal nitrogen of dietary origin: $A = I - (F - F_m)$. The value of $F_m$ is customarily determined by measuring the excretion of nitrogen while the individual is being fed a protein-free diet. The assumption is that subsequent feeding of nitrogen will not alter this value of $F_m$. Digestibility (D) can then be calculated as follows: $D = A/I$.

Digestibility is a very important factor in determining the nutritive value of a dietary protein. For example, raw egg has an antitryptic factor that slows up digestion in the small intestine. Ordinarily this factor is inactivated by gastric juice; however, in dogs depleted in protein stores, inactivation does not occur so that digestion, absorption, and retention of raw egg protein are poor. A similar poor digestibility of raw egg protein has been reported in puppies. Cooking the egg denatures the antitryptic factor, thereby improving the digestibility and nutritive value of egg protein in these animals. Proper cooking in the presence of water also improves the digestion and nutritive value of soybean protein, possibly by denaturing similar factors and by altering the protein. As a result, methionine and other amino acids are liberated more rapidly, providing a better over-all pattern for absorption.[8] Overheating, particularly in the absence of water, can also reduce the nutritive value of proteins by destruction of essential amino acids or by tying them up in new chemical linkages not susceptible to enzymatic digestion.

### Nitrogen Balance Index

One of the most valuable ways of estimating the nutritive value of absorbed nitrogen is to measure the rate (K) of change of nitrogen balance ($\Delta B$) with respect to absorbed nitrogen ($\Delta A$), the rate being expressed as follows: $\frac{\Delta B}{\Delta A} = K$.

The rate (K) called the nitrogen balance index of absorbed nitrogen is a function of the efficiency of retention of nitrogen for anabolism.[9] Nitrogen balance indexes for absorbed nitrogen are illustrated graphically in figure 1, which shows nitrogen balances produced in dogs fed various amounts of different proteins. The series of curves, originating at a negative balance of –4 Gm. per day per square meter of body surface area, present data obtained while feeding various proteins to dogs with full protein stores. Since the tissue stores are full, catabolic activity is high in these animals. The amount of nitrogen needed to maintain nitrogen equilibrium is relatively high—approximately 4 Gm. per day per square meter of body surface area for egg protein, 5.2 Gm. for beef, 5.5 Gm. for casein, 7.1 Gm. for soybean, and 9.1 Gm. for wheat gluten. In figure 1 the curves are linear through-

TABLE 2.—*Nitrogen Balance Indexes for Absorbed Nitrogen Determined for Six Proteins*[a]

| Subject | Egg Powder | Egg White | Beef | Casein | Peanut Flour | Wheat Gluten |
|---|---|---|---|---|---|---|
| Man, adult ..... | 0.94 | 0.91 | 0.67 | 0.68 | 0.56 | 0.42 |
| Dog, adult ..... | 0.87 | 1.14 | 0.77 | 0.73 | 0.56 | 0.44 |
| Rat, adult ..... | 0.82 | 0.94 | 0.69 | 0.51 | 0.46 | 0.65 |
| Rat, growing .... | 0.87 | 0.94 | 0.76 | 0.69 | 0.54 | 0.40 |

[a] From Allison.[8]

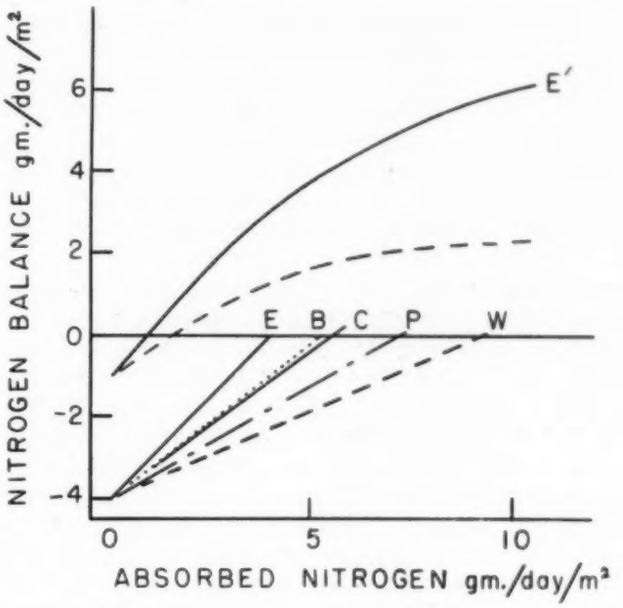



Fig. 1.—Relationship between nitrogen balance and absorbed nitrogen in adult dogs with full protein stores fed the following protein sources: egg, E; beef, B; casein, C; peanut flour, P; and wheat gluten, W. E' and the dash line represent data obtained while feeding protein-depleted dogs proteins of high and low nutritive value respectively.

out the region of negative balance, and the slopes, which are the nitrogen balance indexes, are constant. Under these conditions the catabolism of tissue protein may be constant and independent of nitrogen intakes. If this is true, then the indexes become the fraction of absorbed nitrogen retained in the body of the animal, a fraction defined as the "biological value" of the dietary proteins. This concept of biological value has been developed in detail by Mitchell,[10] who has contributed much to our understanding of the utilization of dietary nitrogen by the body.

The nitrogen balance indexes (biological values) of the six proteins for maintenance in man,[11] dog, and the rat [12] are recorded in table 2. The index for egg protein is close to unity, which can be interpreted to mean that all of the absorbed nitrogen is retained for synthetic purposes, since the pattern of amino acids absorbed is adapted to anabolism. Cystine is not considered an essential amino acid, but, because of the interrelationship between methionine and cystine, the reference pattern for the two are recorded together in table 1. Methionine can be used for the biosynthesis of cystine. Similarly, phenylalanine can be converted into tyrosine, thereby correcting a deficiency of tyrosine if such a deficiency is present in the dietary protein source. Comparing the pattern for egg protein with the reference patterns for growth, the conclusion could be reached that there are excessive amounts of some of the amino acids for protein anabolic needs.

Indexes greater than 0.7 represent a protein of relatively high nutritive value. The lower index of beef and casein may be associated primarily with a small deficiency in sulfur amino acids needed in relatively large amounts in rats and dogs. Adding an optimum amount of methionine to casein increases the index to unity or to slightly above that for egg protein. The very low value for wheat gluten is primarily due to a low lysine content. Adding an optimum amount of lysine increases the index in dogs to 0.74 the value obtained for casein. Obviously, when a protein such as unsupplemented wheat gluten is fed to an adult dog to maintain equilibrium, less than half of the nitrogen fed can be retained for anabolism, and the rest of the amino acids are catabolized, thus increasing the excretion of urea nitrogen. The index for wheat gluten in the adult rat, on the other hand, is of the same order of magnitude as the value for casein. This high value for maintenance in the rat has been interpreted by Mitchell [13] to mean that this animal can synthesize sufficient lysine to meet the requirement for maintenance; the low index for growth (0.4) would mean that lysine cannot be synthesized adequately for growth. Thus the dietary pattern of amino acids needed by the animal may vary with the physiological state. The data would indicate, however, that the pattern for synthesis of tissue proteins for growth or repletion of depleted tissues is essentially the same for man, dog, and the rat.

TABLE 3.—*Uptake and Retention of $S^{35}$ from Methionine in Normal and Depleted Tissues in the Rat*

| Tissue | Diet | $S^{35}$* 1† | 8† | 15† |
|---|---|---|---|---|
| Liver | 18% Casein | 196 | 144 | 82 |
| Liver | Protein-free | 192 | 311 | 143 |
| Heart | 18% Casein | 191 | 98 | 85 |
| Heart | Protein-free | 204 | 198 | 192 |

* All units in micrograms per gram of protein.
† Time after injections, days.

The amount of dietary protein needed for maintenance in humans fed an ideal pattern of amino acids has been estimated to be approximately 0.5 Gm. per day per kilogram of body weight. Using this value the requirements for maintenance expressed as grams of protein per day per kilogram of body weight would be: egg powder, 0.53; egg white, 0.55; beef, 0.75; casein, 0.74; peanut flour, 0.90; and wheat gluten, 1.2. The value of 1 Gm. of protein per day per kilogram often recommended for maintenance in an adult is based on an average diet containing protein varying between peanut flour and casein in nutritive value. Also in the recommendation the provision of sufficient nitrogen for building the protein stores adequately is considered. However, simply to increase nitrogen intake of a poor protein to meet requirements for equilibrium, which could be done, for example, by feeding 1.2 Gm. of wheat gluten per day per kilogram of body weight, does not mean that the physiology of the animal is kept at optimum. Feeding a large quantity of a protein of poor pattern for anabolic needs may increase some of the essential amino acids much above requirements, thereby creating imbalances that can alter the development of tissues. The effects of imbalances, particularly in rats fed a low nitrogen intake have been demonstrated by Elvehjem.[6b] Some of the gross effects of amino acid imbalance may actually be the result of competition for passage across cell membranes before anabolism can take place. The limitation of protein anabolism by faulty dietary patterns, regardless of nitrogen intake, will be revealed further in the following data.

One way to determine the degree of depletion of protein stores in an adult is to determine the degree of positive nitrogen balance that can be produced by a given nitrogen intake, since the greater the depletion the greater the positive balance. Most species, including man, do not ordinarily have full stores; hence, they can be put more or less into positive balance until those stores are filled maximally. Curve E′ in figure 1 records the data obtained after feeding various amounts of egg protein to a dog badly depleted of protein stores. The labile protein stores were reduced in this animal; catabolic activity was low; and very little nitrogen was needed to maintain the depleted state. By feeding egg protein, a high positive balance was obtained, showing a great potential for anabolic activity to replenish the depleted stores. Repletion by feeding a poor pattern of amino acids is illustrated by the broken curve, such data being obtained while feeding different amounts of protein of low nutritive value. No matter how much of this protein was fed, the nitrogen stores could not be filled so rapidly as with egg protein. Repletion with a deficient protein such as wheat gluten did not fill the stores so uniformly as did egg protein, resulting in an animal with an imbalance in tissue proteins. In general, the nitrogen-balance index for a given pattern of amino acids is higher in the depleted than in the normal animal, a fact which has been interpreted to mean that the reduction in over-all catabolic activity in the depleted state is associated with an increased potential anabolic activity. Such an interpretation is supported by the increased retention by various depleted tissues of radioactive sulfur ($S^{35}$) from methionine labeled with this isotope (table 3).

## Growth

The curves in figure 1 have been interpreted to mean that the anabolic efficiency of wheat gluten is much less than that of egg white, no matter how much of the wheat gluten is fed. The data showing positive balances were obtained in animals depleted of protein in which the dietary protein was called upon to promote anabolism of repletion. The amino acid requirements for repletion are similar to those for growth of new tissues in the young. The data in table 4 illustrate the relative protein anabolic efficiencies of egg powder,

TABLE 4.—*Body Weight Gain per Nitrogen Intake, and Nitrogen Balance per Gram of Nitrogen Intake in Beagle Puppies During Fast-Growing Period**

| Protein Source | Body Weight Gain/ Nitrogen Intake | Nitrogen Balance/ Nitrogen Intake |
|---|---|---|
| Egg powder | 9.0 | 0.50 |
| Casein | 9.8 | 0.43 |
| Wheat gluten | 8.8 | 0.18 |

* From Allison.[9]

casein, and wheat gluten for growth.[9] These ratios were obtained while feeding puppies sufficient food to obtain approximately the same body weight gain per gram of nitrogen intake in an attempt to produce maximum anabolic activity with a poorer protein such as wheat gluten. The data demonstrate that the puppies fed the egg powder gained more nitrogen than those fed casein and that the nitrogen gain in animals fed wheat gluten was very low. The animals fed the wheat gluten diet were fat but restricted in development of soft tissues, whereas those fed the egg protein were lean and muscular. If the amino acid pattern is too deficient in certain of the essential amino acids, increasing the nitrogen intake of the deficient pattern will not promote protein anabolism to the extent obtained with a better pattern. Indeed, feeding larger amounts of the deficient pattern produces an imbalance between fat and lean body mass, resulting in deficiences in some tissue proteins. With our present knowledge, it is difficult to establish a dividing line that would make a simple increase in food intake a safe correction for low nutritive value. The body, however, does have great adaptive abilities to correct for dietary errors, and possibly a general rule for calculating protein intake would be as follows: If the biological value of the dietary protein is greater than 60% of the values obtained for egg or milk proteins, the protein intake may be increased

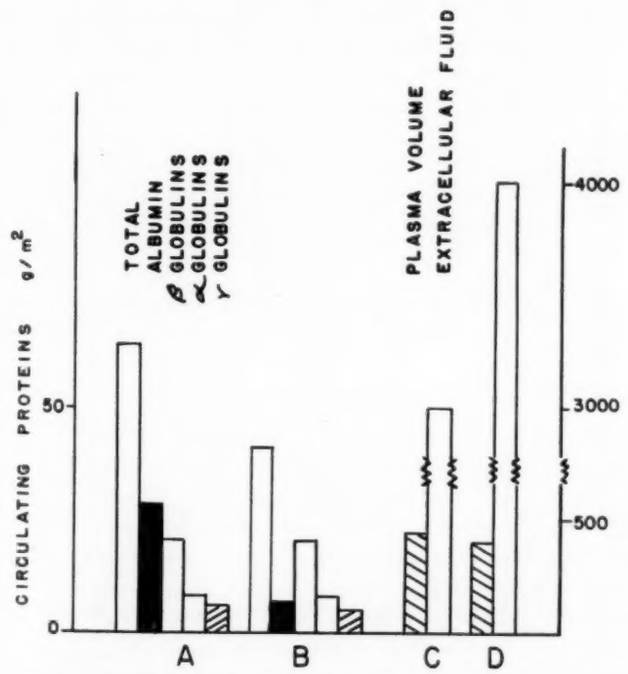



Fig. 2.—Circulating proteins in normal dogs (*A*) and in protein-depleted dogs (*B*), together with plasma volume and extracellular fluid in normal animals (*C*) and depleted animals (*D*). Data from Allison.[14]

to obtain the maximum anabolic activity of the protein. This should be done in such a way that the proper balance between caloric and protein intakes is maintained. If the biological value of the dietary protein is 60% or less than values obtained for egg or milk proteins, the pattern should be improved by supplementation. This supplementation can often be done by proper mixing of various foods or food proteins, helping to correct the amino acid imbalance of the other. Supplementation would be particularly important to correct the diet of infants in whom the requirements for essential amino acids per kilogram of body weight may be 10 or more times the requirements for maintenance in the adult.

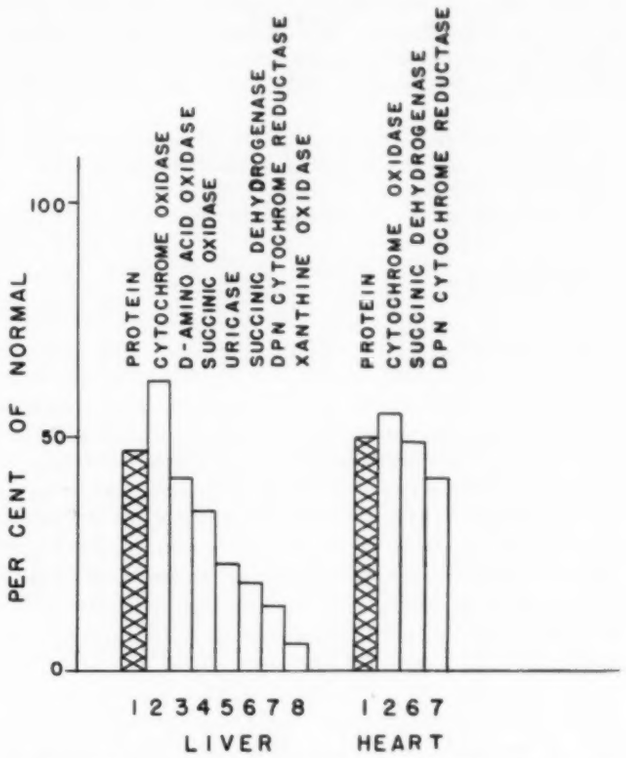



Fig. 3.—Enzymatic activities in the liver and heart of protein-depleted rats. Data from Allison.[14]

### Imbalance of Protein Stores

The imbalance in protein stores that develops as a result of protein deficiencies can be illustrated by the shifts that take place during a period of feeding of a low-nitrogen or protein-free diet. Changes that develop in the circulating plasma proteins of individuals depleted in protein stores are illustrated by the data in figure 2. The plasma albumin is reduced; plasma volume drops; and extracellular fluid increases. Total circulating globulins are not decreased greatly and may even increase, particularly in the presence of some debilitating conditions. Usually the concentration of plasma proteins decreases, resulting in a hypoproteinemia of depletion. Sometimes the fall in plasma volume is so great that, despite the reduction in total circulating proteins, the concentration is still within so-called normal variation.

The greatest imbalance associated with depletion is usually observed in the liver. Here many, possibly most, of the labile protein stores are enzymes, concentrations of which can be described in terms of enzymatic activity as in figure 3.[14] Some enzymes, such as xanthine oxidase, are greatly reduced in activity; others, like cytochrome oxidase, may be increased relative to the total liver protein. This imbalance in the liver results in altered liver function, which can be detected in many ways. One of the most dramatic is to

measure the ability of the liver to detoxicate some toxic substance like 2-fluorenamine. This compound is acetylated in the liver of dogs and progressively oxidized, becoming more and more polar until final breakdown into oxidized products. The excretion of a heat-labile, water-soluble derivative has been taken as a measure of the degree of detoxication; the more of this intermediate product excreted, the less complete the detoxication. The effect of dietary casein concentration upon acetylation and detoxication of 2-fluorenamine in dogs is illustrated in table 5.[15] Animals fed the diet free of protein developed the typical imbalance in enzyme systems associated with depletion and, under these conditions, excreted 2.4 mg. of the heat-labile amine. Feeding precisely the amount of casein needed to maintain nitrogen equilibrium in these animals (6.3% casein) reduced the excretion of the amine to 1.3 mg. The diet fed these animals contained vitamin B complex in amounts thought to be adequate for growth. Increasing the pantothenate concentration increased the activity of the liver enzyme involved in acetylation of the amine, leading to an increased excretion of the acetylated product and a reduction in the excretion of the heat-labile intermediate oxidation product. Complete elimination of this intermediate product was obtained after feeding a relatively high-protein diet supplemented with riboflavin, evidently by stimulating the synthesis of liver enzyme systems. Thus effective doses of anesthetics, chemotherapeutic agents, and other medicines may vary greatly with the physiological state of the labile protein stores.

TABLE 5.—*Effect of Dietary Casein Concentration on Acetylation and Detoxication of 2-Fluorenamine in Dogs**

| Dietary Casein, % | Acetylated Amine | Water-Soluble, Heat-Labile Amine |
|---|---|---|
| 0 | 0.05±0.01 | 2.4±0.1 |
| 6.3 | 0.05±0.01 | 1.3±0.1 |
| 6.3 + Pantothenate | 0.36±0.07 | 0.4±0.2 |
| 25 | 0.12±0.01 | 0.9±0.2 |
| 25 + Riboflavin | 0.11±0.01 | 0 |

* From Allison.[15] All units in milligrams per kilogram of body weight.

## Caloric Intake

The proper correlation of caloric with protein intake is important to develop maximum anabolism with the desired proportions of fat to lean body mass. Certain general principles are evolving from various studies between caloric and protein intakes that may be reviewed briefly.[16] There is an optimum caloric intake for maximum protein anabolism, but it varies with protein intake and with the physiological state of the individual. Reducing the calories somewhat below this optimum increases protein catabolism, increasing the quantity of dietary nitrogen needed for maintenance of equilibrium; however, it need not alter the efficiency of utilization of dietary amino acids for anabolism. The data can be interpreted to mean that the individual catabolizes some of the amino acids of the body pool when ingested calories are restricted. A large reduction in calories depletes the protein stores rapidly, but, as the stores decrease, the caloric requirements seem to decrease. The individual also becomes adapted to some extent to the restricted diet.

The data plotted in figure 4 illustrate the response of dogs in various physiological states to caloric restriction. The bars over *A* in this figure illustrate the effect on nitrogen balance of a decrease in caloric intake in dogs fed a constant protein intake. The nitrogen balance decreased in value as the caloric intake was reduced from 3,190 to 2,860 and to 480 calories per day per square meter of body surface area, becoming negative in animals fed the lowest caloric intake. These results illustrate the increased catabolism and loss of nitrogen associated with caloric restriction. Further data suggest that, as the protein stores are increased, catabolic activity increases and caloric requirements are higher. The latter are maximum when the stores are completely filled. Thus, when calories are restricted in an animal with full protein stores, the animal dips deeply into these stores, thereby greatly increasing the excretion of nitrogen. The negative nitrogen balance over *B* in figure 4 was obtained in a dog with full protein stores that was fed 480 calories per day per square meter of body surface area. On the other hand, if the stores are low, catabolic activity is low and the caloric requirements seem to be minimum. Therefore, positive nitrogen balance was produced in a depleted dog (see *C*, fig. 4) fed the same amount of protein and the same low amount of calories fed to dog *B*. Restricted caloric intake for the depleted animal, however, will eventually result in irreversible tissue damage.

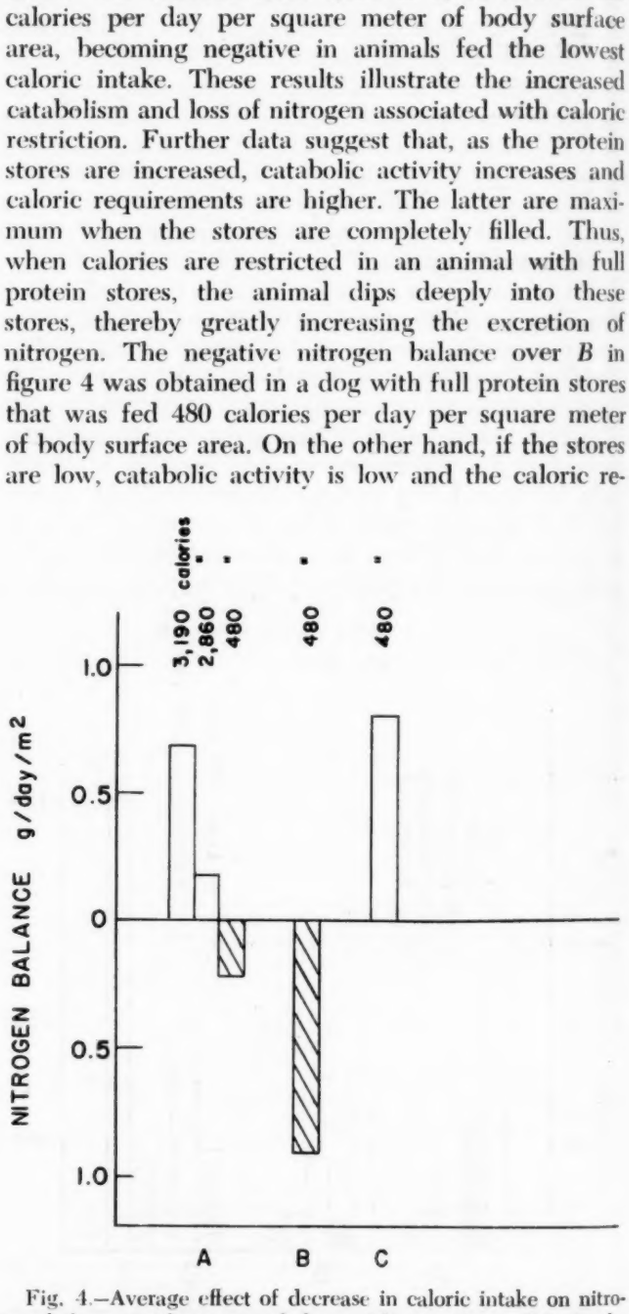



Fig. 4.—Average effect of decrease in caloric intake on nitrogen balance in three normal dogs with constant protein intake (*A*), in a dog with full protein stores (*B*), and in a dog with depleted stores (*C*). Data from Allison.[14]

## Summary

This review of protein nutrition and metabolism emphasizes the dynamic state of the labile protein stores. These stores are the blood and tissue proteins that increase or decrease in quantity as the dietary nitrogen is raised or lowered respectively. The essentiality of certain amino acids in the diet for maximum growth of the tissues is emphasized, giving certain guide lines to help estimate the nutritive value of various dietary protein sources. The concept is developed that protein stores are continually being broken down through catabolism, thereby providing energy and amino acids for the metabolic pool. This pool may be particularly important to provide energy and essential amino acids during periods of malnutrition associated with sickness, stress, or low food intake.

A proper balance between amino acids, furnished by the diet and the body reserves, and all other constituents in the diet would be required for maximum welfare of the body tissues. Reduction in caloric intake, for example, increases the utilization of body protein reserves for energy purposes. Many tissue proteins are parts of enzyme systems, with their coenzymes of inorganic ions and/or vitamin complexes. Thus protein malnutrition may produce symptoms characteristic also of caloric, vitamin, or mineral deficiencies. This survey of the metabolic contour map, incomplete as it is, emphasizes the role that all dietary constituents play in the development of these contours. The use of amino acids and associated metabolites to alter abnormal contours toward normal is an important and obvious development in nutritional therapy.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**X-Ray Accuracy.**—The accuracy of roentgen examinations of the chest was appraised in comparison with autopsy findings in 254 cases with gross chest disease who died within a reasonably short time after filming. The objective phase of roentgen interpretation, or rate of demonstrability of intrathoracic lesions, was found to vary proportionately to the diversification of examination techniques from 63 per cent adequacy for frontal projections only through 73 per cent for projections in two or more planes to 100 per cent for fluoroscopy combined with assorted films. When all films of unsatisfactory technical quality were excluded, the adequacy rates increased to 68 per cent, 87.5 per cent and 100 per cent respectively. The subjective component or personal equation was then investigated and failed to improve with greater adequacy of examinations. However, the most objective possible reinterpretation of the original reports disclosed that in 52 cases a correct diagnosis should have been but was not made from the available films. The original rate of accuracy of interpretation was 44 per cent but became 65 per cent when correction was made for errors in initial interpretation of adequate examinations. Ninety-two per cent of all examinations consisted of frontal projections only, one-fourth of which were bedside films, and the majority of patients were too ill to permit adequate roentgen studies. Finally, the effect of the nature and location of 432 lesions upon their demonstrability by various types of examinations was reviewed, confirming that demonstrability varies essentially in proportion to the complexity of filming techniques.—J. T. Littleton III, M.D., and J. H. Feist, M.D., The Accuracy of Roentgen Examinations of the Chest, *The Guthrie Clinic Bulletin*, October, 1956.

# THE JOURNAL
## OF THE AMERICAN MEDICAL ASSOCIATION

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## HISTORY-MAKING EVENT IN MEDICAL COMMUNICATION

On the morning of June 5, history will be made in the field of medical communication. That day, through arrangements made by Smith, Kline & French Laboratories, two of the world's great medical confraternities —the physicians of the United States and of Great Britain—will be linked for more than an hour via the new underseas cable. This "joint meeting" of the American Medical Association, then in annual session in New York, and the Harvey Tercentenary Congress, convened in London on the 300th anniversary of the death of William Harvey, will hear distinguished panelists on both sides of the Atlantic exchange information on cardiac surgery.

This is a notable, exciting part of the medical profession's "person-to-person" program, urged last fall by President Eisenhower. And it is fitting that Harvey is the subject of this truly international conference. His work is itself an example of the internationalism of science.

Circulation of the blood is so basic a part of current medical thought that sometimes we forget the importance of Harvey's contribution unless we recall medical doctrine as it stood at the time of the Renaissance. This doctrine held that the liver was the center of circulation, and that the heart merely contained air, or blood mixed with air, which left the right side through invisible pores in the ventricular septum. Air, passing through the arteries, conveyed "animal spirits" *(animus)* to parts of the body. The veins, and the veins alone, contained blood. The 20th century medical historian Castiglioni has stated that the correction of this concept constituted in the Renaissance "the fulcrum of all physiological knowledge; in fact, one cannot speak of true progress in physiology until the secret of circulation was revealed—a secret that had challenged attention since classical times without having resulted in much progress."

Harvey's challenge was bold and accurate. In 1628, he wrote in his monumental "De motu cordis": "It is absolutely necessary to conclude that the blood in the animal body is impelled in a circle, and is in a state of ceaseless motion; that this is the act or function which the heart performs by means of its pulse, and that it is the sole and only end of the motion and contraction of the heart."

In arriving at this "absolutely necessary" conclusion, Harvey had solved various parts of the puzzle of circulation by inductive physical demonstrations. But he had as a foundation the work of great names in Renaissance medicine. There was Vesalius, a Fleming of German origin, who in 1543 disputed the permeability of the ventricular septum; there was the Spaniard Michael Servetus, who in 1553 stated a rough hypothesis of the pulmonary aeration of the blood, and there was the Italian Fabricus d'Aquapendente, Harvey's own teacher at Padua, who in 1603 elaborately described the valves of the heart. To the spread of knowledge in the Renaissance there were no international "curtains"; indeed, one Renaissance expert has written of "new reciprocal relations between members of the European group of nations" as a vital characteristic of the Renaissance itself. Thus, the work of Vesalius and Servetus was freely available to Harvey—as was the opportunity to study in Italy under Fabricus, perhaps the greatest surgeon of the day.

Nor does internationalism end there with the theory of circulation. Harvey's book was published on the Continent—in the free city of Frankfurt. The entire world of late-Renaissance science—Italy, France, Germany, Scandinavia, the Lowlands and England—entered into the controversy that followed publication of "De motu cordis." And in the end, the work of many men of different locales—Aselli of Cremona, Jean Pecquet of Dieppe, Malpighi of Bologna—added incontrovertible facts of physiology to Harvey's own findings.

It may be fair to say that the lack of nationalism in Renaissance science set the pattern of internationalism that generally characterizes modern science. Just as this internationalism long predated current international "curtains," we believe that it will long outlast them.

And perhaps that last statement explains in part why the President's request for a "person-to-person" program in the medical sciences is so important in terms of international understanding. The many scientific journals, the many international meetings, and free correspondence by men interested in the same search—these provide already-established avenues by which any free nation can prove its goodwill. So it is that on June 5, when two medical meetings will be linked, two nations will be linked. Not only will science be served, but free men everywhere.

## TOP FOREIGN FILMS—AN A. M. A. "FIRST"

The estimated 18,000 physicians gathering in New York City for the American Medical Association's Annual Meeting June 3-7 will have a rare opportunity to see some of the finest aspects of foreign medical practice.

During the last three and a half days of the convention, 40 outstanding medical motion pictures from abroad will be shown in the Barbizon Plaza hotel. This will combine postgraduate education with audiovisual delight, according to representative specialists who have previewed the films during the past five months. Subjects range from blastomycosis to volvulus. Film-running time varies from 10 to 53 minutes. The 15 countries represented reach from Japan to Czechoslovakia, from Brazil to Australia.

It will be the first time in the A. M. A.'s 106 annual meetings that American physicians will be able to watch foreign colleagues at work via an international exhibit of medical films. Almost all the scenes are in color, and all will be presented in English. Here is another example of organized medicine recognizing the impact of audiovisual techniques on mass audiences of the profession. It ranks with the previous A. M. A. convention "firsts" of live color telecasts in 1949, scientific exhibits in 1899, and amplified broadcast of human heartbeats.

The A. M. A.'s office of Motion Pictures and Medical Television (under the Council on Scientific Assembly) has arranged the program so that individual film showings will dovetail with section meetings on the same subject. For example, films on pediatrics will be screened prior to section meetings on pediatrics; movies relating to surgery will be shown in the morning, while the section meeting on surgery will take place that same afternoon.

Already, several state medical associations and specialty groups have requested reshowings for their members during the six months that the 16-mm films will remain in this country. They will be loaned on a first-come-first-served basis. The same rule will apply for hospitals, medical schools, and county societies that request the dozen or so motion pictures that the A. M. A. will include in its permanent film library.

There is such great technical interest in these presentations that scores of cinematographers, producers, and audiovisual experts from abroad and many parts of the nation are attending the A. M. A. meeting specifically to study details of photography, animation, and directing. The microscopic photography is described as "superior." One film from Japan, on the structure and function of the middle ear, is characterized by several otologists who have seen it as the finest presentation on hearing concepts ever shown.

This program, presented with the cooperation of Johnson & Johnson, also includes a symposium June 6 on problems in the international exchange of medical motion pictures. There will be no repeat presentations of any of the films at the meeting, and seating capacity is limited to 500 per showing. Physicians are therefore urged to plan their attendance in advance by consulting their official program as well as listings in the daily bulletin.

Medical and surgical films speak an international language. Now American doctors, gathered together, will be able for the first time to grasp this world-wide communication in its very essence.

## ORGANIZED HOME CARE PROGRAMS

Recently there has been increased attention to the supplying of medical services through what are termed "home care programs." At the very beginning there must be a clear differentiation between home care as has always been provided by the private physician and "organized" home care, in which there are coordinated efforts under a central administration that supplies the medical and paramedical services as part of what might be termed a "team effort."

The practice of medicine in the United States has always been primarily a home care program in which a physician treated illness in the home where possible, and, at the same time, called upon nursing, social, and rehabilitative services and resources, as he felt they were needed. The family physician has an additional advantage, however, in that, being a personal physician, he also knows which services will actually be utilized, and not merely accepted. For example, when he considers occupational therapy he must judge the receptiveness of the patient. Furthermore, he does not attempt to change nutritional habits without adequate preparation of the patient or those responsible for the care of the patient. In short, his knowledge of the "whole" patient and the family environment assists him in properly organizing his own team.

Despite the advantages of treatment in a home, there were still many patients who required hospitalization. As the shortage of hospital beds increased and as the cost of hospital care rose, especially for prolonged illness, many physicians began selecting certain patients who would not require all the facilities of a hospital and began amplifying their treatment in the home. Paralleling this comprehensive medical care, a few organizations developed "home medical services," "hospital extended care programs," and other similarly named services. No matter what they were called, they all served to provide central administration for the coordination of various medical and related services to meet the health needs of the patient and his family.

Because of the expressed interest, not only by the medical profession but by the public as well, the Committee on Indigent Care of the A. M. A. Council on Medical Service conducted a survey designed to obtain basic information on organized home care programs in the United States. Sooner or later, local medical societies will be involved either directly or indirectly with such medical care. It is felt that an understanding of the programs now in operation will be their best guide in evaluating how they will respond if such a program is begun in their own community. The report of the survey prepared by the A. M. A. committee appears on page 298 of this issue.

What started out as primarily a chronic illness program for the indigent has developed into home-hospital services for patients with acute illness and those who are convalescing. Such organized home care programs are promoted by the sponsoring organizations as one of the best means of providing for the medical, social, and rehabilitation needs of certain patients as well as being the total medical care plan for certain groups. No attempt has been made to evaluate the programs now in operation, but it does seem that, as more and more "organized" programs begin to appear, it becomes more and more the responsibility of the practicing physician to assume his share in the planning and administration of such forms of medical care. This should allow the physician, who in the long run directly supplies the predominant service and in essence assumes the responsibility for total medical care, to match his responsibility with authority, and it will at least attempt to prevent the practice of medicine by those who have not graduated from medical school.

# ORGANIZATION SECTION

## MEDICOLEGAL SYMPOSIUMS

More than 1,000 doctors and lawyers from 44 states attended the 1957 American Medical Association medicolegal symposiums presented in Atlanta, Ga., March 15-16; Denver, March 22-23; and Philadelphia, March 29-30. These meetings marked the second time that a series of joint meetings between the medical and legal professions has been sponsored by a national organization. The A. M. A. sponsored the first such series in October, 1955, at Chicago, Omaha, and New York City.

Dr. David B. Allman, A. M. A. President-Elect, opened the meetings in Atlanta and Philadelphia. Dr. George F. Lull, A. M. A. Secretary and General Manager, opened the meeting in Denver. Local medical society and bar association officials also welcomed the participants at each meeting.

Both A. M. A. speakers laid particular emphasis on the need for cooperation between the legal and medical professions, and both noted with satisfaction that the A. M. A. and the American Bar Association national meetings last year featured speeches on medicolegal cooperation from the presidents of the A. B. A. and A. M. A. respectively.

Dr. Allman outlined four areas in which cooperation between the two professions is needed, i. e., preparation and use of doctors who must testify in court; control of narcotics addition and care for addicts; enactment of the Jenkins-Keogh bill, or similar legislation to provide tax deferments for the self-employed on funds to be set aside for retirement purposes; and development of an interprofessional code of understanding for the two professions.

Each symposium was devoted to three general topics. These were as follows:

1. Chemical Tests for Intoxication. Under this section the drunken driving problem was analyzed. It was generally agreed that the medical and legal professions can do much to reduce highway traffic deaths by encouraging the widespread use of chemical tests in all suspected violations involving drunken driving. The importance of chemical intoxication test evidence being accepted by the courts was stressed. Experts also testified that use of tests not only would convict the guilty but would absolve the innocent of guilt as well. Cases were cited in which death had occurred in persons who were jailed overnight for suspected drunkenness, when actually they were suffering from a head injury or an acute diabetic condition. Participants agreed that chemical tests could have prevented these tragedies.

2. Trauma and Cancer. The second day of each meeting began with a panel discussion on the topic of trauma and cancer. The medical panelists reported that a single trauma cannot cause cancer. In each case, however, there was at least one attorney who "proved legally" that a single trauma may cause cancer. Nearly all of the speakers agreed that court decisions are, in most cases, lagging behind accepted medical findings on the relationship of trauma to cancer. They also agreed that attorneys, judges, physicians, and lawmakers should direct their efforts toward correcting the common practice of awarding large settlements in cases where trauma is claimed as a cause of cancer but is not scientifically proved as such.

The physicians and attorneys at the three meetings who spoke on this subject were:

*Atlanta*—William F. Martin, New York City, attorney, moderator; Theodore J. Curphey, M.D., Hempstead, N. Y.; Paul J. Grotzinger, M.D., Philadelphia; and Hugh G. Head Jr. and A. Walton Nall, Atlanta, attorneys.

*Denver*—Alan R. Moritz, M.D., Cleveland, moderator; A. Reynolds Crane, M.D., Philadelphia; William F. Martin, New York City, attorney; and Charles J. Traylor, Grand Junction, Colo., attorney.

*Philadelphia*—William F. Martin, New York City, attorney, moderator; I. S. Ravdin, M.D., Philadelphia; Russell S. Fisher, M.D., Baltimore; Elwood S. Levy, Philadelphia, attorney; and Kraft W. Eidman, Houston, Texas, attorney.

Hugh G. Head, who appeared on the Atlanta program, commented on the doctor's responsibility for testifying in court, saying, "it is the duty of the doctor basically to aid and heal the sick and . . . it is a fair inference that it is also the duty of the doctor to be very careful about denying this sick and injured human the prosthetic appliance of the courtroom."

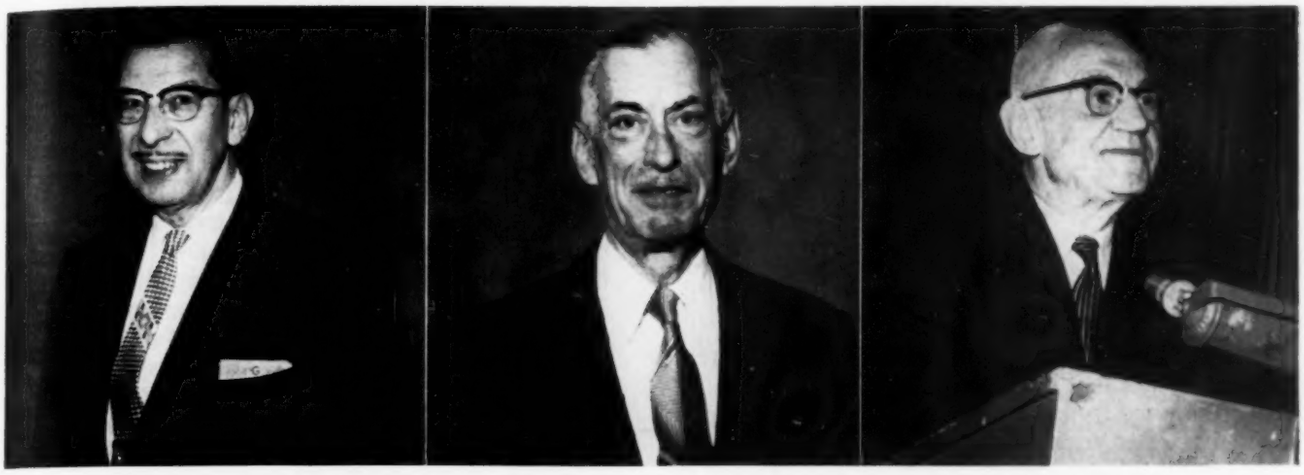
3. Medical Expert Testimony. It was decided in the discussion on medical expert testimony that joint responsibility on the part of the doctor and the lawyer in examining the facts, examining the patient, and preparing or "briefing" testimony beforehand could prevent most cases of miscarried justice in medicolegal suits. Lectures and panel discussions pointed out that the most frequent errors by attorneys in this regard are "over-cross-examination" of medical expert witnesses, failure to properly prepare and qualify medical witnesses, and failure to let the doctor know what sort of questions to expect under cross-examination. Doctors, on the other hand, err most often by exhibiting tendencies to arrogance and hostility under cross-examination, by failing to become thoroughly familiar with the medical facts in the case, and by failing to translate the medical history brought out under examination into terms that can be readily understood by the jury.

Irving Goldstein of Chicago, attorney, author, educator, and editor, spoke at Atlanta and Philadelphia on "Medical Expert Testimony." Kenneth W. Robinson, veteran trial lawyer, handled this part of the program at Denver.

Each symposium ended with a question-and-answer session between the audience and a panel of medicolegal experts. The participants in these panels were as follows:

*Atlanta*—Irving Goldstein, moderator; Edgar F. Fincher, M.D., Emory University, Georgia; Theodore S. Raiford, M.D., Asheville, N. C.; and Hamilton Lokey and Edgar A. Neely Jr., Atlanta, attorneys.

*Denver*—Kenneth M. Wormwood, Denver, attorney, moderator; Charles G. Freed, M.D., Denver; William M. Krigsten, M.D., Sioux City, Iowa; Fred J. O'Connor, Chicago, attorney; and Godfrey Nordmark and Lawrence M. Wood, Denver, attorneys.



*Left*, Irving Goldstein, Chicago attorney, spoke on "Medical Expert Testimony" at the Atlanta and Philadelphia meetings. *Center*, Dr. David B. Allman, Atlantic City, N. J., A. M. A. President-Elect, welcomed the groups in Atlanta and Philadelphia and called for a four-point program of cooperation between the medical and legal professions. *Right*, Dr. Herman A. Heise, Milwaukee, spoke on "Chemical Tests for Intoxication."

*Left*, C. Joseph Stetler and Capt. Robert F. Borkenstein before the camera in the mock court trial demonstration. A television news feature was sent to 211 U. S. stations early in March, focusing attention on the symposiums and calling attention to the value of chemical tests for intoxication. *Right*, mock trial demonstration showed how to put theory into practice, particularly in the prosecution of drunken driving cases. Left to right, Edwin J. Holman and Mr. Stetler, A. M. A. Law Department; Captain Borkenstein, Indiana State Police; and William J. McAuliffe Jr., A. M. A. Law Department, taking test.

Opening the symposium at Denver with speeches of welcome were (left to right) Joseph G. Hodges, Denver, president, Colorado Bar Association; Dr. George R. Buck, Denver, president, Colorado State Medical Society; Thomas M. Burgess, Colorado Springs, member, Board of Governors, American Bar Association; and Dr. George F. Lull, Chicago, Secretary-General Manager, A. M. A.

*Philadelphia*—Irving Goldstein, moderator; Robert M. Bernstein, Philadelphia, attorney; Philip H. Strubing, Philadelphia, attorney; Fred J. O'Connor, Chicago, attorney; Abraham M. Ornsteen, M.D., Philadelphia; and Daniel F. Featherston, M.D., Asbury Park, N. J.

A mock court trial prepared by C. Joseph Stetler, Head of the A. M. A. Law Department, was presented on the afternoon of the first day, after a discussion by Dr. Herman A. Heise of Milwaukee, who spoke at all three meetings on "Chemical Tests for Intoxication—Scientific Background and Public Acceptance." Dr. Heise, chairman of the A. M. A. medicolegal subcommittee on chemical tests for intoxication, called attention to the fact that half of the 40,000 traffic fatalities in 1956 resulted from what he termed "alcohol flavored accidents." His remarks elicited favorable editorial comment from a number of newspapers in all parts of the nation. Among these was an editorial by Bert Struby, editor of the Macon *Telegraph*, a Georgia newspaper. Editor Struby wrote:

> His [Dr. Heise's] comments turn the spotlight again on a matter which today concerns too few citizens in our state but which in the future, by its own gravity, is going to demand public consideration and action.
>
> Speaking at a forum of doctors and lawyers last weekend, Dr. Heise pointedly accused alcohol of being the greatest single factor in automobile accidents. Yet, he said, legal proof of intoxication is extremely difficult without evidence such as that obtained in chemical tests.

The mock court trial served to put theory into practice by example. With the inexorable drama spelled out in the step-by-step process of law in the courtroom, the fate of one Warren A. Drinker, accused of driving while under the influence of alcohol, was sealed.

The two-hour demonstration presented a formidable case for the use of breath tests for intoxication. The testimony of a medical expert witness, the arresting officer, a police technician who tested the culprit's breath at the time of arrest, and finally the testimony of the defendant himself, all served to illustrate dramatically the points made by Dr. Heise. The trial proved to be an excellent example of the legal process as it must be coordinated with medical science in order to bring about just verdicts in cases where the establishment of much fact depends upon the skillful presentation of technical scientific data.

The actors in the demonstration were as follows:

Expert Medical Witness, William W. Bolton, M.D., Associate Director, A. M. A. Bureau of Exhibits, Chicago; Police Technician, Capt. Robert F. Borkenstein, Indiana State Police, Indianapolis; Arresting Officer, Sgt. G. Herbert Williams, Atlanta Police Department, Georgia; Defendant, George B. Larson, Assistant Director, A. M. A. Bureau of Exhibits, Chicago; Prosecuting Attorney, Edwin J. Holman, A. M. A. Law Department, Chicago; Defense Attorney, William J. McAuliffe Jr., A. M. A. Law Department, Chicago; and Judge, C. Joseph Stetler.

The cast of the demonstration trial remained the same for the Denver and Philadelphia symposiums, with the following exceptions:

*Denver*—Arresting Officer, Sgt. Thomas O'Neill, Denver Police Department; Prosecuting Attorney, Warren E. Whyte, A. M. A. Law Department, Chicago; and Defense Attorney, Frank W. Barton, Secretary, Council on National Defense, A. M. A., Chicago.

*Philadelphia*—Expert Medical Witness, Dr. Herman A. Heise, Milwaukee, and Arresting Officer, Capt. Maurice Pliner, Philadelphia Police Department.

"The Medical Witness," a 30-minute motion picture produced by the W. S. Merrell Company, with the cooperation of the American Medical Association and the American Bar Association, was shown at each symposium. The film gives both good and bad examples of courtroom technique. It also warns against many of the pitfalls encountered in medicolegal trials.

The symposiums were, in effect, a short course designed to bring doctors and lawyers to a better understanding of the responsibilities and interdependence of both professions in the administration of justice. C. Joseph Stetler, Head of the A. M. A. Law Department, said that another series will be presented in 1959 in the East, the Middle West, and the West.

*The two following items are from the March, 1957, Bulletin of the Joint Commission on Accreditation of Hospitals (600 N. Rush St., Chicago; Kenneth B. Babcock, M.D., director) and are reproduced below for the information they contain that will be of interest to many physicians.*—Ed.

## STANDARDS FOR HOSPITAL ACCREDITATION

During 1956, in keeping with the policy of the Joint Commission on Accreditation of Hospitals, the Standards for Hospital Accreditation were under continued study and evaluation. This is to insure a dynamic, progressive program established within a framework of solid basic principles with sufficient flexibility to encourage initiative and allow for a maximum of freedom in the implementation of the Standards. Any change in the Standards made by the Board of Commissioners as a result of such study is predicated on its effectiveness to safeguard the patient and improve the quality of medical care in hospitals. After such study and thoughtful deliberation, the Board of Commissioners, at its meeting in December, 1956, modified Standard II B 4b, concerning attendance at medical staff meetings. The old Standard reads as follows:

"Active Staff attendance shall average at each meeting at least 75 percent of the active staff who are not excused by the Executive Committee for just cause. Each active staff member shall attend 75 percent of staff meetings unless excused by the Executive Committee for just cause."

The new Standard reads:

"Active Staff attendance shall average at each meeting at least 50 percent of the active staff who are not excused by the Executive Committee for just cause. Each active staff member shall attend 50 percent of staff meetings unless excused by the Executive Committee for just cause."

The modification of this Standard was recommended by the Committee on Standards which was charged by the Board of Commissioners to consider the "Conclusion of the Stover Report."* The Board of Commis-

*"Staff meetings required by the Joint Commission are acceptable, but the attendance requirement should be set up locally and not by the Commission."

sioners voted to accept the recommendation of the Committee on Standards for the following reasons:

1. A well functioning medical staff with good intercommunication is essential to insure quality medical care.

2. The general staff meeting is an important tool both as an administrative and educational device to keep the staff as a whole informed of hospital activities and to insure continuity of good medical practice.

3. It is essential that every hospital have rules and regulations pertaining to attendance at medical staff meetings. In order to make certain that these rules are adequate, the Commission should furnish a specific yardstick in the Standards.

Medical staffs and administrators should realize that this new modified Standard supersedes, as of publication in this Bulletin, the former 75 percent attendance requirement. The different types of staff meetings or categories to be employed as explained in prior Bulletin No. 9 should be reviewed thoroughly. The surveyors of the Joint Commission have been instructed to look carefully at the performance of medical staffs as regards review of work performed in the hospital.

## REPORT OF ACTIVITIES—1956

ACCREDITED HOSPITALS

| | December 31, 1956 | December 31, 1955 |
|---|---|---|
| TOTAL | 3770 | 3630 |

NUMBER OF SURVEYS CONDUCTED IN 1956

| | |
|---|---|
| TOTAL | 1421 |
| U. S. & Possessions | 1299 |
| Canada | 120 |
| Foreign | 2 |

RESULTS OF SURVEYS CONDUCTED IN 1956

| | | |
|---|---|---|
| TOTAL | 1421 | 100% |
| Accredited for three years | 1043 | 73.4% |
| Accredited for one year | 261 | 18.4% |
| Not accredited | 117 | 8.2% |

### In Review

Many letters are received each month at the offices of the Joint Commission on Accreditation of Hospitals which show considerable lack of knowledge of the basic structure and program of our organization. For informational purposes a few of the facts are reiterated.

1. The Joint Commission is a voluntary non-profit organization supported solely by contributions from its member organizations. Their names are listed on the mast head. No charge is made for a survey of any hospital.

2. Before applying for a survey for accreditation a hospital must be eligible. The eligibility rules are simple and as follows:

a. The hospital must have functioned for at least one year in its present capacity.

b. The hospital must have at least 25 adult beds.

c. The hospital must be listed by the American Hospital Association. For listing, application should be made directly to the American Hospital Association. Listing and accreditation are not synonomous, nor are they done simultaneously. Listing comes first, then accreditation. Any hospital, religious, private, nonprofit, governmental or proprietary institution which fulfills the eligibility requirements may apply for accreditation.

3. After a hospital applies for accreditation one month to one year may elapse before the hospital can be surveyed. Schedules for surveys are made up at least two months in advance and once made usually cannot be changed. Hospitals are notified usually two to three weeks in advance of the survey date. Because of travel conditions, hospitals in the south generally are surveyed in winter and those in the north in summer.

4. After a survey the report is mailed to the office of the Joint Commission by the surveyor or his member organization. The surveyor's report contains his written recommendations for the improvement of patient care. The staff of the Commission reviews the surveyor's report, any correspondence about the hospital, and the report of the previous survey to determine what action has been taken with respect to the recommendations made. The recommendations of the surveyor and the staff are sent to each Commissioner, who approves or disapproves them. The hospital is notified of the official action of the Commission. The whole process takes from 60 to 90 days. If the recommendations are disapproved by even one Commissioner the report to the hospital in question is held over until the Commissioners' meeting, when a vote is taken and a majority prevails.

a. Hospitals approved for three years are entitled to a Certificate. The hospital will automatically be resurveyed in approximately three years.

b. Hospitals approved for one year are not entitled to a Certificate and must return the previous Certificate if they have one. They will be automatically resurveyed in approximately one year.

c. Hospitals which are not accredited must re-apply for survey if and when they feel that the standards can be met.

d. Dry runs or trial surveys by the Commission staff cannot be made. Neither the money nor personnel is available.

e. Only physicians are employed to survey hospitals. A great deal of an accreditation survey has to do with the quality of care and only a physician can attempt to assess this care.

5. The "Standards" of the Joint Commission are its basic document and every hospital medical staff, administrative staff and board of trustees should be acquainted with its contents. Bulletins of the Commission are published approximately every four months and contain for the most part interpretations and explanations of the Standards, plus other statistical information.

Multiple copies of all basic publications may be purchased for a nominal fee. A copy of every Bulletin is sent free to the administrator and the chief of staff of each hospital. It is their duty to see that essential information in the Bulletin is passed on to the medical staff and key personnel.

6. The primary and controlling purpose of the Joint Commission on Accreditation of Hospitals is to insure that the best possible quality care is provided in hospitals and to encourage improvement of patient care as rapidly as knowledge and experience permits.

This purpose is the natural result of the underlying philosophy of the accreditation program. The philoso-

phy that hospitals must be evaluated from the point of view of the patient. In plain words "Is this hospital giving good quality care to the extent that I am willing for a member of yours or my family to be a patient in the hospital?"

Accreditation is not compulsory either on the the part of the hospital or the accreditation body. It is not licensure. It is not government enactment. Accreditation is a voluntary effort on the part of every hospital, its medical staff, its board of trustees and its administration to raise the quality of patient care.

## NATIONAL SCIENCE FAIR

The American Medical Association participated in the eighth National Science Fair in Los Angeles, May 9-11, by presenting citations to the four high school students with the best exhibits in the basic medical sciences. The presentations were made at a special A. M. A. banquet for 600 Fair participants—students, advisors, and representatives of organizations sponsoring regional science fairs—Friday evening, May 10, at the Biltmore Hotel. Dr. Dwight H. Murray, A. M. A. President, made the awards and invited the two "first place" citation winners to be guests of the A. M. A. at its Annual Meeting in New York City, June 3-7. They will display their exhibits in the Scientific Exhibit in the Coliseum.

The keynote speaker at the banquet was Dr. Wendell M. Stanley, professor of biochemistry and director of the virus laboratory at the University of California in Berkeley. John Howard, star of "Dr. Hudson's Secret Journal," a weekly network television program, was master of ceremonies. Entertainment was provided by several Hollywood personalities.

The recipients of the A. M. A. citations were selected by a special committee from the Association. Committee chairman was Dr. Alphonse McMahon, St. Louis, Chairman of the A. M. A. Council on Scientific Assembly, and members of the committee were Drs. Samuel P. Newman, Denver; Stanley P. Reimann, Philadelphia; Henry Viets, Brookline, Mass.; and Thomas G. Hull, Chicago, all members of the Council; and Dr. Donald A. Charnock, president of the California Medical Association, and Dr. J. Norman O'Neill, president of the Los Angeles County Medical Association.

The National Science Fair is the culmination of local and regional science fairs in which finalists from all over the United States compete for national honors. It is sponsored by Science Clubs of America to stimulate interest among high school students in the pursuit of science as a career. The A. M. A. House of Delegates last June resolved to "bring the whole of organized medicine into active participation in this worthwhile and constructive program to encourage the youth of our nation to take a serious interest in the field of science." During the past two years, a great number of county and state medical societies and their woman's auxiliaries have assisted in the development and promotion of community high school science fairs.

## A. M. A. SPONSORS MEDICAL CIVIL DEFENSE CONFERENCE

The A. M. A. Council on National Defense has completed program arrangements for its Fifth Annual National Medical Civil Defense Conference, to be held Saturday, June 1, in the Sert Room of the Waldorf-Astoria, New York City. The conference is to be devoted to the medical aspects of the hazards and effects of radiation and radioactive fall-out.

This is the second such conference held on the topic of radiation hazards, according to Mr. Frank W. Barton, Council Secretary. Several years ago, the A. M. A. Board of Trustees directed the Council to regularly inform physicians about the radiation and radioactive fall-out hazards. The first conference devoted to this subject was held in June, 1955, at Atlantic City. At hearings conducted by a subcommittee of the House Committee on Government Operations on the subject of civil defense for national survival, Mr. Barton said that witnesses of the Naval Radiological Defense Laboratory testified they are convinced, on the basis of their studies, that radioactive fall-out must be considered "the major antipersonnel weapon."

Physicians wishing to attend the conference should make advance registration for the meeting and luncheon by promptly writing to the Council on National Defense, American Medical Association, 535 N. Dearborn St., Chicago 10.

### FIFTH ANNUAL NATIONAL MEDICAL CIVIL DEFENSE CONFERENCE

JUNE 1, 1957—NEW YORK, NEW YORK
SERT ROOM—WALDORF-ASTORIA

*Sponsored by*

*Council on National Defense*
*American Medical Association*

PROGRAM COMMITTEE

Carroll P. Hungate, M.D., Chairman
Cortez F. Enloe Jr., M.D.
Harold C. Lueth, M.D.

| | | |
|---|---|---|
| 9:00- 9:05 | **Call to Order and Introductory Remarks** | Dr. Hungate |
| 9:05- 9:15 | **Welcome Address in Behalf of A. M. A.** | Dr. Allman |
| 9:15- 9:30 | **Federal Civil Defense Affairs** | (Administrator FCDA) |
| 9:30-10:00 | **Civil Defense—A Program of Federal Responsibility** | Mr. Holifield |

| | | | |
|---|---|---|---|
| 10:00-12:15 | **Meeting Radiation Hazards—FCDA Programs and Plans** | | |
| | 10:00-10:30 | Radiological Briefing | Mr. Greene |
| | 10:30-11:00 | Shelter Briefing | Mr. Taylor |
| 11:00-11:15 | **Break Period** | | |
| | 11:15-12:15 | Medical Care | Dr. Van Sandt |
| 12:30- 2:00 | **Luncheon—Empire Room** | | |
| 2:00- 3:30 | **Effects of Radiation** | | |
| | 2:00- 2:30 | Biological Changes—Total Body Exposure | Dr. Cronkite |
| | 2:00- 2:30 | Utilization of Nagasaki and Hiroshima Casualty Studies | Mr. Corsbie |
| | 3:00- 3:30 | Animals, Animal Products, and Crops | Dr. Comar |
| 3:30- 4:30 | **Medical Management—Radiation Casualties** | | |
| | 3:30- 4:00 | Military Concepts | General Cooney |
| | 4:00- 4:30 | Civilian Concepts | Dr. Howland |
| 4:30- 5:00 | **FCDA Film "Treatment of Nerve Gas Casualties** | | Colonel Stewart |
| 5:00- 5:15 | **Summary and Roundup** | | Dr. Enloe |

The Council has arranged for the FCDA to display a radiologic exhibit which will be monitored by Mr. Fred Oleson, Radiological Defense Officer, Region I, Federal Civil Defense Administration, Harvard, Massachusetts.

**Participants**

DAVID B. ALLMAN, M.D., President-Elect, American Medical Association, Atlantic City, N. J.

JAMES P. COONEY, Major General, M. C., U. S. A., Deputy Surgeon General, Department of the Army, Washington, D. C.

ROBERT L. CORSBIE, Division of Biology and Medicine, Atomic Energy Commission, Washington, D. C.

CYRIL COMAR, Ph.D., Chief, Biomedical Research, Oak Ridge Institute for Nuclear Studies, Oak Ridge, Tenn.

EUGENE P. CRONKITE, M.D., Head, Division of Experimental Pathology, Medical Department, Brookhaven National Laboratory, Upton, Long Island, N. Y.

CORTEZ F. ENLOE JR., M.D., Member, Committee on Civil Defense, Council on National Defense, American Medical Association, New York.

JACK C. GREENE, Director, Radiological Defense Division, Health Office, Federal Civil Defense Administration, Battle Creek, Mich.

HONORABLE CHET HOLIFIELD, U. S. Congressman, 19th District of California, Chairman, Sub-committee on Military Operations, Committee on Government Operations, Washington, D. C.

JOSEPH W. HOWLAND, M.D., Chief, Medical Division, Atomic Energy Commission Project, University of Rochester, Rochester, N. Y.

CARROLL P. HUNGATE, M.D., Member, Committee on Civil Defense and Council on National Defense, American Medical Association, Kansas City, Mo.

FRED OLESON, Radiological Defense Officer, Region I, Federal Civil Defense Administration, Harvard, Massachusetts.

FRANCIS B. STEWART, Colonel, U. S. A. R., Consultant, Chemical and Biological Warfare Defense, Health Office, Federal Civil Defense Administration, Battle Creek, Mich.

BENJAMIN C. TAYLOR, Director, Engineering Office, Federal Civil Defense Administration, Battle Creek, Mich.

M. M. VAN SANDT, M.D., Director, Medical Care Division, Health Office, Federal Civil Defense Administration, Battle Creek, Mich.

## INTERNATIONAL ASPECTS OF NEW YORK MEETING

At every Annual Meeting of the American Medical Association there are several hundred physicians from other countries in attendance. Never before, however, have so many foreign guests been on the program as there will be in New York this year. More than a score of countries will be represented. A Trans-Atlantic Medical Conference will be presented for the first time, with a two-way telephone connection between London and New York. The occasion is the Harvey Tercentenary Congress. Sir Clement Price Thomas

Sir Clement Price Thomas, moderator, in London, for the Trans-Atlantic Medical Conference.

will head a distinguished panel in the Great Hall at the Royal College of Surgeons, while Dr. Michael E. DeBakey will be in charge of a similar group in Carnegie Hall, New York. Audience participation at both ends will be encouraged. The program is presented with the cooperation of Smith, Kline & French Laboratories, Philadelphia.

Another "first" at the New York meeting will be the International Medical Film Exhibition, with four full days of outstanding motion pictures produced in other countries. Never before have so many excellent films representing medical progress been gathered together. Many of the authors of the films will be present to discuss their work. All discussions will be in English. The program is presented with the cooperation of Johnson & Johnson, New Brunswick, N. J. Other leading physicians from abroad will lecture before the sections or present their work in the Scientific Exhibit. In addition, more than 2,000 physicians and scientists from the United States will participate in the program, to make the New York meeting an outstanding contribution to graduate medical education.

# COUNCIL ON MEDICAL SERVICE

## ORGANIZED "HOME CARE PROGRAMS" IN THE UNITED STATES

### A REPORT BY THE COMMITTEE ON INDIGENT CARE

The concept of care in the home is not a new one. Home care has always been an integral part of the practice of medicine in this country; a method whereby the sick person could be attended and relieved of his illness without separation from his family environment.

More recently, however, increased attention has been focused on what are being termed "home care programs," in which selected patients who do not require all the treatment facilities of a hospital, but who would otherwise have to be hospitalized, are provided with a range of individualized medical, nursing, social, and rehabilitative services in their own homes, coordinated through one central agency.

There has been growing interest in these programs, not just as a substitute for hospital care but as that part of a total medical care plan which can best meet the needs of certain patients or of a given patient in certain phases of his illness. It is in view of this increased interest that the Committee on Indigent Care of the Council on Medical Service conducted a survey designed to obtain basic information on the origin and purposes, organization, administrative mechanics, and the advantages and problems encountered in the operation of such home care programs currently under way in the United States.

The findings of this survey are reviewed here. No effort has been made to evaluate the home care programs now in operation, nor is this report to be considered as either an approval or a disapproval of such programs. However, it is believed that the data included here will be helpful to those medical societies concerned with this type of medical care program.

### The Survey

The Committee's first step was to arrive at a working definition of an organized home care program, as contrasted to those instances in which a patient receives, in his home, the services of a physician who may call individually upon a nurse, a social worker, a therapist, or a homemaker to assist him. Background material for this purpose was drawn from the files of the Commission on Chronic Illness, which had compiled many data on the subject, from a survey of 11 home care programs conducted in 1952 by the Public Health Service of the U. S. Department of Health, Education and Welfare in cooperation with the Commission on Chronic Illness,[1] and from other material in the files of the Committee on Indigent Care.

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Members of the Committee on Indigent Care are Drs. John F. Burton, Chairman, Oklahoma City; A. J. Bowles, Seattle; E. P. Coleman, Canton, Ill.; Wesley W. Hall, Reno, Nev.; I. Jay Brightman, Albany, N. Y.; E. A. Ockuly, Toledo, Ohio; Dean W. Roberts, Chicago; and Mr. R. M. Hilliard, Consultant, Chicago.

For the purposes of the survey, an organized home care program was defined as "one in which selected patients while homebound are provided with a full range of services which are arranged for and coordinated through one administrative agency or institution; one in which home care, as part of a total medical care plan, meets patients needs . . . during a specific phase, or phases of illness." [2]

A home care program, as such, was expected to include at least the minimum of medical and nursing care, social services, and essential drugs and supplies. It was expected that many of the programs surveyed would report additional services, such as physical or occupational therapy, homemaking, health education, and nutritionist services. The essential characteristics of an organized home care program were considered to be (1) centralization of responsibility for administration, (2) coordination of the various services and resources made available to the patient, and (3) the development and use of the medical care team or the opportunity for various disciplines to deal jointly with the health needs of the patient and his family and to develop definitive planning for the patient. In addition, the program was required to be served by one or more hospitals, with adequate facilities and equipment for extending services into the home.[3]

On June 29, 1956, a seven-page questionnaire was mailed to all organizations which had been noted in available literature as having this type of program. These organizations were queried as to the origin, purpose, administration, patients served (by types of illness, financial status, and referral sources), number and type of services offered to the patient at home, personnel and administrative mechanics of the program, sources of financing, and advantages and problems encountered in the operation of the program. On Aug. 13, another copy of the questionnaire was mailed with a follow-up letter to those organizations which had not replied. Cut-off date on returns was Sept. 30, 1956.

From a total of 69 questionnaires mailed, 51 were returned. The questionnaire returned by the New York City Department of Hospitals covered the operation of its home care program in 14 municipal hospitals which had been queried individually in the survey. Thus 65 of the 69 organizations queried were accounted for in the returns as follows: 24 respondees indicated no home care program or that their program had been discontinued, and 27 organizations reported a home care program currently in operation. Of these 27 replies, 5 were deleted from the study: 3 in which medical care and medicaments only were provided, one in which patients were placed in nursing homes rather than their own homes, and one in which insufficient data were given. The remaining 22 programs, in addition to 9 others on which data had been ob-

tained for 1951-1952,[1] or a total of 31, are the subject of this report, and are hereafter referred to as the programs (table 1).

## Origin and Purposes

At the time of the survey, five programs were operating on a pilot or demonstration basis, that is, to demonstrate the practicality of such a program and the degree to which it might meet community needs. Three of these programs had been in operation less than a year, one for 14 months, and one for 21 months. Three programs were in the process of transition from a demonstration to a continuing basis: one of these had been operating for a year, one for three years, and one for four years.

One organization, the Boston Dispensary of the New England Medical Center, has been providing home care services since 1796. Another organization, the Massachusetts Memorial Hospitals, has been operating a home medical service since 1875. The University of Vermont has operated a home care program since 1925, and the Chicago Department of Welfare has been providing home medical services as part of its over-all assistance program since 1933. Of the remaining 19 programs, one had been in operation for over 15 years, one for over 10 years, 9 for over 5 years, 7 for over 2 years, and one for slightly less than 2 years.

There was some variation in the reported objectives and purposes of the various programs, but, with a few exceptions, the objectives seemed to revolve around

TABLE 1.—*Home Care Programs in the United States*

| | Program* | Address | Date Established | Services Given in the Home‡ |
|---|---|---|---|---|
| California | (1) Alameda County Tuberculosis Home Care Program† | Fairmont Hospital of Alameda County, San Leandro. | July, 1949 | abc ijkl |
| | (2) San Francisco Home Care Program | Mt. Zion Hospital, 1600 Divisadero, San Francisco. | Jan., 1956 | abcdefghijkl |
| Colorado | (3) General Medical Clinic | Denver General Hospital, W. Sixth Ave. and Cherokee St., Denver 4. | June, 1953 | abc gh jkl |
| Connecticut | (4) Greater Hartford Home Care Program | Greater Hartford Community Council, Hartford. | June, 1956 | abcdefghi kl |
| Washington, D. C. | (5) D. C. Department of Public Health HCP | Gallinger Municipal Hospital, Washington. | April, 1950 | abc ijkl |
| | (6) Georgetown University Medical Center Home Care Service for Cancer Patients | Georgetown Univ. Hospital, 38th and Reservoir Road N.W., Washington. | March, 1950 | abcde ghijkl |
| Illinois | (7) Mt. Sinai Home Medical Care Program | Mount Sinai Hospital, 2750 W. 15th Pl., Chicago. | Dec., 1952 | abcd ghijkl |
| | (8) Mercy Clinics Home Medical Care Program | Mercy Clinics, 2526 S. Calumet Ave., Chicago 16. | March, 1952 | abcde ghijkl |
| | (9) Home Medical Service of Michael Reese Hospital | Mandel Clinic, Michael Reese Hospital, E. 29th and S. Ellis, Chicago. | 1949 | abcde ghijkl |
| | (10) Chicago Dept. of Welfare† | Chicago Department of Welfare, Chicago. | 1933 | abcd ghijkl |
| | (11) Peoria Home Care Plan of the V. N. A. | Visiting Nurse Association, 823 Main St., Peoria. | Aug., 1955 | abcdefghi kl |
| Massachusetts | (12) Boston Dispensary Home Medical Service | Tufts University School of Medicine, 25 Bennet St., Boston. | 1796 | abcd ghijkl |
| | (13) Massachusetts Memorial Hospitals Home Medical Service† | Boston University School of Medicine, Boston. | 1875 | abcd ghijkl |
| | (14) Department of Home Care, Beth Israel Hospital | Beth Israel Hospital, 330 Brookline Ave., Boston. | Sept., 1954 | abcde ghijkl |
| Michigan | (15) Home Care Demonstration of Detroit | Visiting Nurse Association, 51 W. Warren Ave., Detroit. | July, 1955 | abcdefghijkl |
| Minnesota | (16) St. Mary's Home Nursing Service | St. Mary's Hospital, 1216 S.W. Second, Rochester. | Sept., 1943 | abc ghijkl |
| Missouri | (17) Home Care Dept. Jewish Hospital of St. Louis | Jewish Hospital of St. Louis, 216 S. Kingshighway, St. Louis 10. | June, 1953 | abcde hijkl |
| New Jersey | (18) Mountainside Hospital Home Care Program | Mountainside Hospital, Montclair. | Jan., 1954 | abcdefghijkl |
| New York | (19) N. Y. C. Department of Hospitals Home Care Program<br>(Bellevue)<br>(City)<br>(Coney Island)<br>(Cumberland)<br>(Fordham)<br>(Goldwater)<br>(Gouverneur)<br>(Greenpoint)<br>(Harlem)<br>(Lincoln)<br>(Kings County)<br>(Metropolitan)<br>(Morrisania)<br>(Queens General)<br>(Triboro) | N. Y. C. Department of Hospitals, 125 Worth St., New York 13. | Nov., 1948 | abcdefghijkl |
| | (20) Montefiore Hospital Home Care Program† | Montefiore Hospital, Bronx. | 1947 | abcde ghijkl |
| | (21) The Home Care Program for Cancer Patients | Bronx Hospital, Fulton Avenue at 169th Street, Bronx. | Jan., 1954 | abcd fghijkl |
| | (22) Extra-Mural Care Program of the Home for Aged and Infirm Hebrews, New York | Home for Aged and Infirm Hebrews, 121 W. 105th St., New York 25. | April, 1948 | abc e ghijkl |
| | (23) Genesee County Health Department HCP | Genesee County Health Dept., Batavia. | 1953 | abcd g ijkl |
| Ohio | (24) Home Medical Service | Jewish Hospital, Burnet Avenue, Cincinnati. | May, 1950 | abcd ghijk |
| | (25) The Benjamin Rose Institute† | Benjamin Rose Institute, Cleveland. | 1940 | abcde hijkl |
| Pennsylvania | (26) Philadelphia Home Care Program† | Visiting Nurse Society of Philadelphia, Philadelphia. | April, 1949 | abcdefghijkl |
| | (27) Montefiore Hospital Home Care Program | Montefiore Hospital, Pittsburgh. | Aug., 1952 | abcdefghijkl |
| | (28) The Home Care Program of the Albert Einstein Medical Center, Lucien Moss Home | Albert Einstein Medical Center, York and Tabor roads, Philadelphia 41. | June, 1955 | abcdefghijkl |
| Vermont | (29) University of Vermont Home Care Program† | University of Vermont, Burlington. | 1927 | abcdefghijkl |
| Virginia | (30) Richmond Home Medical Care Program† | Richmond Department of Public Health, Richmond. | July, 1949 | abcd ghijkl |
| Washington | (31) King County Hospital Extension Service† | King County Hospital, Seattle. | July, 1952 | abcdefg ij l |

* The figures in parentheses will be used to identify individual plans in subsequent tables and will be referred to as program numbers.
† Data in report obtained for year 1951-1952.
‡ a, medical (visiting physician and/or consultation); b, nursing; c, social service; d, physical therapy; e, occupational therapy; f, speech therapy; g, health education; h, housekeeping service; i, hospital equipment and supplies; j, medicaments and medical supplies; k, orthopedic appliances; and l, transportation.

the concept of home care as the most satisfactory means of meeting the total care needs of certain patients or of a patient during certain phases of his illness. In the different programs this concept was extended to (1) patients convalescing from acute illness or acute exacerbation of chronic illness, (2) patients too sick or disabled to come to an outpatient clinic but not sufficiently sick or disabled to be in a hospital, (3) chronically ill and/or the indigent who did not require hospital care, (4) patients who were occupying hospital beds solely because a more suitable place for care was lacking, and (5) patients whose psychological and emotional needs would be more readily met, with recovery made more quickly, if their family environment could be maintained.

Only one of the programs was established primarily as a teaching experience for medical and other student personnel, but eight of the sponsoring organizations reported this activity as one of the purposes or part of the current operation of the program. Without exception, the organizations including professional or student education in their program cited the excellence of home care as a teaching experience in the family setting.

Some of the programs were established primarily to offset a shortage of hospital beds, as an alternative to the high cost of hospital care for the indigent and medically indigent, and for other specific reasons. However, there was a growing acceptance throughout the survey returns of home care not just as a way to save money or as a substitute for hospital care or as a new way of training professional personnel but as the best means of providing for medical, social, and rehabilitative needs of certain patients or of an individual patient during certain phases of his illness, and as an important part of a total medical care plan for certain groups.

In general, then, the somewhat overlapping objectives, cited by the founding organizations, in establishing a home care program were (1) to provide the indigent and medically indigent with a quality of care and a range of services not normally available to this group, and at less cost; (2) to shorten the length of stay of hospital patients and reduce the readmission of discharged patients by providing better follow-up care at home; (3) to bridge the gap in medical care for those patients too ill to visit an outpatient clinic but who do not need hospital care; (4) to meet the needs of a growing number of chronically ill and/or aged patients who do not require institutional care but are occupying institutional beds because a more suitable place for care is lacking; (5) to speed the recovery of those patients to whom the family environment would have a therapeutic effect; (6) to offer the homebound patient a coordinated spectrum of medical, social, and rehabilitative services individualized to his particular needs; (7) to afford medical, nursing, and other professional and student personnel with a teaching experience in environmental medicine; and (8) to provide the private family physician with a single source from which he can obtain a comprehensive array of nursing, social, and rehabilitative services for his patient.

In all of the programs studied, including those on a demonstration basis, the sponsoring organizations felt that the original purposes of the program had been or were in the process of being fulfilled.

### Administration and Organization

In one program, operating on a pilot basis at the time of the survery, the administrative and coordinative duties were carried on by an independent committee which was created specifically for that purpose, and which did not itself provide any direct services to patients. In this program, administrative responsibility was delegated to an executive committee composed of representatives from the county medical society and six other local health, welfare, and service organizations. This committee worked with a medical advisory board consisting of representatives from six medical specialties in determining medical policies.

In all of the remaining programs the administrative agency participated to some extent in direct services to patients. This participation varied from a hospital-based program in which the administrative agency provided 11 of 13 different home services, to a program administered by a private social agency which provided only social casework services and arranged for 12 other patient services through existing community facilities. Thirteen of the remaining 30 programs were administered by general hospitals or by departments of general hospitals. One of these was established as a separate entity but was based at a general hospital, insofar as the director of the hospital was also the director of the home care program and the hospital provided some of the patient services.

One program was administered jointly by a general hospital and a chronic disease unit. Four were administered jointly by a medical school and a general hospital, three by chronic disease hospitals, and one by a university medical school. Three programs were administered by visiting nurse associations. In two of these, administrative and coordinating responsibilities were delegated to the director of the visiting nurse association, who set up over-all program policies under the guidance of a steering committee and with the help of a medical coordinator. In the third program, administrative responsibility was vested in a public health nurse coordinator who worked full time on the program under a board of directors and with the guidance of a medical advisory committee and a professional advisory committee in setting program policies.

Three programs were administered by health departments: one by a public health department in close affiliation with a municipal hospital; one by a city health department in cooperation with a state medical college; and one by a county health department as a part of its over-all health program.

In two other organizations also, home services were given only as a part of an over-all health program. One of these programs was administered by a city welfare department as part of its over-all general assistance program to city indigents. The other was carried on by a private social agency as one facet of its over-all health assistance program for needy older people. Table 2 gives a brief description of the administrative organization in all programs.

TABLE 2.—*Administrative Agency—All Programs*

(1) Administered by the Alameda County (Calif.) Department of Institutions—based at the Fairmont Hospital of Alameda County, a chronic disease hospital.

(2) Established as a separate entity but based at the Mt. Zion Hospital, a voluntary nonprofit general hospital, insofar as the director of the program is also director of the hospital and some of the patient services emanate from the hospital. Program maintains a close, though informal, working relationship with Chronic Illness Service Center and other service groups in San Francisco.

(3) Administered jointly by the University of Colorado Medical School and the Denver Department of Health and Hospitals. Based at the General Medical Clinic of Denver General Hospital. Home care services provided as part of over-all educational-service program to Denver indigents in hospital, home, or outpatient clinic.

(4) Established as a separate entity and administered by an executive committee composed of a physician-chairman, who is medical administrator of the program, and representatives from the Hartford County Medical Association, City Health Department, Visiting Nurse Association, Hartford Rehabilitation Center, Family Service Society, Junior Chamber of Commerce, and social service departments of local hospitals.

(5) Administered by the Bureau of Disease Control of the D. C. Department of Public Health, and based at the D. C. General Hospital.

(6) Administered by the Georgetown University Hospital, a church-affiliated general hospital in Washington, in cooperation with the Georgetown University School of Medicine.

(7) Administered by and based at the Mt. Sinai Hospital, a voluntary nonprofit general hospital in Chicago.

(8) Administered by and based at the Mercy Clinics of Mercy Hospital, Chicago, a church affiliated general hospital connected with the Stritch School of Medicine of Loyola University.

(9) Administered by the Babette and Emmanuel Clinic of Michael Reese Hospital, a voluntary nonprofit general hospital.

(10) Administered by the Chicago Department of Welfare. Home care services are given when needed as part of the department's over-all assistance program to the indigent of the city.

(11) Administered by the Visiting Nurse Association in Peoria under the guidance of a medical advisory committee and a professional advisory committee. Program functions essentially as a separate entity.

(12) Administered by the Boston Dispensary, which with the Floating Hospital and the Tufts Medical School makes up the nucleus of the New England Medical Center, which provides clinical experience to Tufts College medical students.

(13) Administered jointly by the Massachusetts Memorial Hospitals, a voluntary nonprofit association, and the Boston University School of Medicine, which is privately endowed.

(14) Administered by the Beth Israel Hospital, a voluntary nonprofit general hospital in Boston.

(15) Administered by the Visiting Nurse Association in Detroit under the guidance of a steering committee that includes members of the Wayne County Medical Society.

(16) Administered by St. Mary's Hospital of Rochester, a church-affiliated general hospital.

(17) Administered by the Jewish Hospital of St. Louis, a voluntary nonprofit general hospital which comprises a part of the Jewish Hospital Center in St. Louis. The program operates as a specific department of the hospital.

(18) Administered by the Mountainside Hospital, a voluntary nonprofit general hospital serving Montclair and 10 other communities in Essex County.

(19) Administered by the New York City Department of Hospitals and operated in 15 city hospitals: 13 general, 2 chronic, and one tuberculosis hospital.

(20) Administered by the Montefiore Hospital, a voluntary nonprofit hospital for chronic disease.

(21) Administered by the Bronx Hospital, a voluntary nonprofit general hospital.

(22) Administered by the Home for Aged and Infirm Hebrews, a voluntary nonprofit chronic disease hospital.

(23) Administered by the Genesee County Health Department as part of its over-all health program and in cooperation with the Genesee Memorial Hospital.

(24) Administered by the Jewish Hospital of Cincinnati, a voluntary nonprofit general hospital.

(25) Administered by the Benjamin Rose Institute, a private social agency which was set up through a trust fund for the care of older people. Home care services are given when needed as part of the institute's total program of assistance to needy older people.

(26) Administered by the Visiting Nurse Society in Philadelphia, under the guidance of a steering committee composed of a part-time medical consultant and representatives from civic and professional groups.

(27) Administered by the Montefiore Hospital in Pittsburgh, a voluntary nonprofit general hospital.

(28) Administered jointly by the Albert Einstein Medical Center in Philadelphia, a voluntary nonprofit general hospital, and the Lucien Moss Home, a nonprofit voluntary chronic disease facility which is physically contiguous with the Northern Division of the Medical Center.

(29) Administered by the University of Vermont School of Medicine, and jointly financed by the School and the City of Burlington.

(30) Administered by the Richmond, Va., Department of Public Health. Program operates in close cooperation with the Medical College of Virginia, which provides some of the patient services and uses the program as a teaching resource.

(31) Administered by the King County (Seattle) Hospital System consisting of two county hospitals. University of Washington School of Medicine uses the program as a teaching resource for medical students.

## Private Physician Participation

In six of the programs, patients were required to have a private physician willing to assume responsibility for their care before they could be admitted to the home care program. The various services and facilities in the program were then coordinated to the request of the individual physician, who decided which services his patient would receive, either alone or after consultation with the medical and professional advisors on the program. If the patient had no private physician at the time of referral to the home care program, he was required to select one from among the practicing physicians in the community.

Three of these private physician–based programs were on a pilot basis at the time of the survey; this included the program which was administered independently of the service-providing agencies, and two of the programs administered by visiting nurse associations. The fourth program was in the process of transition from a pilot to a continuing basis, and was administered jointly by a general hospital and a chronic disease unit. The fifth program had been operating since 1949, and was also administered by a visiting nurse society. The sixth program was administered by a county health department as part of its over-all health program.

Four of these programs were restricted to patients with long-term illness, and two accepted patients with both chronic and acute diseases. All provided services both to the indigent and to patients able to pay, with the latter charged according to their ability to pay.

Two other programs also provided the patient with a free choice of physician, but in a slightly more restricted sense. In one of these, administered by a county chronic disease hospital and serving indigent and medically indigent tuberculosis patients only, the patient selected his physician from a panel maintained by the program. This physician then became responsible for the patient's total treatment and ordered such services as he thought necessary. In the second program, administered by a city department of welfare as part of its over-all assistance program to the indigent, the patient selected a physician from a roster of approximately 1,000 licensed physicians who had expressed a desire to participate in the program. These physicians prescribed such services as they thought necessary for their patients, in consultation with a medical advisory committee, and were paid by the program for medical services on a fee-for-service basis.

In seven of the programs the patient remained under the care of his private physician if he had one, although this was not one of the requirements for eligibility. If the patient had no private physician, he was treated by a physician on the home care staff or panel.

In 15 of the programs patients received medical services only from physicians on the home care staff or medical students participating in the program, who prescribed additional services to the patient as needed, alone or in joint consultation with other members of the home care team. Ten of these programs were hospital-based, three were administered jointly by a hospital and medical school, one by a medical school only, and two by city health departments.

One other hospital-based program, which was established originally for the indigent and medically indigent, also attempted on a pilot basis to care for private patients, retaining the patient's family physician as

head of the medical care team. However, the project was discontinued because payments by Blue Cross and Blue Shield could not be made applicable to care in the home. Table 3 shows the sources of medical services to patients for all programs.

TABLE 3.—*Sources of Medical Services to Patients—All Programs*

| Source of Care | Program Numbers |
|---|---|
| Home care physicians only | (1)* (2) (3) (5) (7) (8) (9) (10)* (12) (13) (14) (18) (19) (20) (24) (27) (30) (31) |
| Private physicians or home care physicians | (6) (16) (17) (21) (22) (25) (29) |
| Private physicians only | (4) (11) (15) (23) (26) (28) |

* Selected by the patient from a panel or roster of physicians maintained by the home care program.

Two of the programs in which the patient could receive home medical services only from physicians on the program staff reported some difficulty in interpreting the program to private physicians in the community and a reluctance on the part of these physicians to transfer responsibility for their patients care.

## Types of Patients

Of the 31 programs, 19 were restricted to indigent and medically indigent patients; of these, 8 served only patients with long-term illness, 11 accepted those with both acute and chronic diseases, and one accepted only tuberculosis patients.

In 12 programs, home services were available to both indigent or medically indigent and paying patients, who were charged according to their ability to pay. Five of these programs were restricted to persons with chronic diseases, five accepted those with both chronic and acute cases, and two were restricted to cancer patients. In five of these programs, indigency was not specifically stated as a requirement for admission, but the majority of the patient case load were indigent or medically indigent, and the program was oriented primarily toward serving this group. Table 4 shows the type of patients served, by financial status, for all programs.

A number of programs specified exceptions within the disease categories accepted for care. Most frequently mentioned was mental illness, which was excepted from eligibility in eight of the programs. Active tuberculosis was not accepted in five of the programs, obstetric cases were not accepted in two programs, one program would not accept patients

TABLE 4.—*Type of Patients Served, by Financial Status, for All Programs*

| Type of Patients | Program Numbers |
|---|---|
| Indigent and medically indigent only | (1) (2) (3) (5) (7) (8) (9) (10) (12) (13) (14) (18) (19) (20) (24) (27) (29) (30) (31) |
| Indigent and paying, but actual case load primarily indigent | (6) (16) (21) (25) (28) |
| Indigent and paying | (4) (11) (15) (17) (22) (23) (26) |

with diabetes, and two would not accept patients with contagious diseases. Table 5 shows the general disease categories eligible for care in all programs.

The following additional criteria for patient eligibility were common to most of the programs: 1. The patient's illness must be of a type medically suitable for home care, i. e., the patient does not need the intensive diagnostic and treatment services of a hospital but needs medical supervision, is too ill to obtain it on an ambulatory basis, and the illness can be adequately cared for in the home without constituting a medical hazard to the rest of the family. 2. The patient's home must be physically suitable for care. 3. There must be a family member or other person available to care for the patient at home. 4. The patient must desire to remain at home, and home environment should be psychologically suitable. 5. The family must want the patient at home, and his presence must not impose undue hardship on other family members.

Almost all of the programs limited their home care services to those patients living within a specified geographical area, for such reasons as staff travel time and expenses, the accessibility to the patient of the central home care agency, and the administrative jurisdiction of the sponsoring agency. The distances to which home care services were extended in the various programs varied from 3 to 15 miles, and would indicate a probable practical limit of about 20 miles or an hour's travel time one way.

In one program, administered by a private social agency as part of an over-all assistance program to the elderly, only men over 65 and women over 60 years

TABLE 5.—*General Disease Categories Eligible for Care—All Programs*

| Categories | Program Numbers |
|---|---|
| Chronic only | (2) (5) (7) (9) (11) (14) (16) (20) (22) (24) (26) (27) (28) |
| Chronic and acute | (3) (4) (8) (10) (12) (13) (15) (17) (18) (19) (23) (25) (29) (30) (31) |
| Specific disease categories only | (1) (6) (21) |

of age, of Anglo-Saxon origin, were eligible for services. In two programs, patients were required to be of Jewish faith.

## Referral Sources

Eleven hospital-based programs accepted patients primarily or solely from wards or the outpatient clinic of the hospital or from affiliated social agencies in one case. One of the programs which was private physician-based accepted referrals only from physicians in the community; another accepted referrals primarily from this source.

Eighteen programs accepted referrals from any agency or individual in the community. In this last group, hospital wards and outpatient clinics constituted an important referral source, whether they were part of the administrative agency in hospital-based programs or under other hospitals in the community. Other important referral sources included physicians, patients and families or relatives, nursing and convalescent homes, visiting nurse associations, and various social, health, and welfare agencies in the community.

The number of patients receiving services during a year's time varied from 3 patients in one of the pilot programs which had been in operation for about two months at the time of the survey to 8,868 patients in the Boston Dispensary program which had been in operation since 1796. Four programs besides the Boston Dispensary had a yearly case load over 1,000.

In the five programs operating on a pilot basis, the patient case loads were comparatively small, ranging from 3 to 56. Most of the remaining programs clus-

tered in a range of between 25 and 100 patients served per year, with a fairly even distribution between these two points.

### Services to Patients

In this survey, the organizations queried were not asked to describe specifically the services given to the patient in his home other than under headings such as "medical," "nursing," and "social." However, using descriptions of this type that were obtained in a previous detailed survey of 11 home care programs,[1] and certain other data obtained in the present survey, it may be of practical value to attempt a description of the specific procedures that such things as home medical services and nursing services might entail.

On the basis of previous information, home medical services may include such procedures as taking case histories, making physical examinations and diagnoses, dispensing and administering routine medicaments given orally or parenterally, taking blood, urine, or sputum specimens for analysis, and other uncomplicated diagnostic and therapeutic procedures, including, in some cases, electrocardiography, determinations of basal metabolic rates, transfusions, and, in some cases, minor surgical procedures and specialist consultation.

Nursing services may include such services ordered by the physician as dressings, injections and irrigations, assisting the physician with such therapeutic procedures as transfusions and surgical procedures, bed baths and other personal care, health instruction to the patient, and teaching other members of the family how to care for the patient.

Social services may include evaluation of the patient's social eligibility for home care, interpretation of the program to patients and family members, helping the family adjust themselves to illness in the home, utilizing community resources to meet family economic needs and social problems not directly related to the illness situation, and maintaining liaison between and coordination of the various other agencies providing home care services.

Physical therapy would include such services as corrective exercise, massage, short wave and ultraviolet treatments, wax therapy, instruction in crutch walking and the use of other prosthetic appliances, and chiropodic care for diabetic patients.

Occupational therapy would include such activities as leather work, basket making, painting, weaving, music and the learning of specific skills and crafts, and would encompass both diversional and occupational therapy.

Speech therapy would include visits as needed by a qualified speech therapist.

Health education may include instruction of the family in caring for the patient, instruction of the patient in personal care, nutritional and meal planning consultation, especially for patients with diabetes, and other related services, usually carried on by a nurse, nutritionist, or social worker.

Homemaker services would include the preparation of meals and menu planning, care of children in the home, marketing, and other domestic work necessary to maintain the home.

Other services which may be provided in a home care program include home teaching for children on the program, medicaments and medical supplies, orthopedic appliances, psychological testing and psychiatric consultation, oxygen and blood, hospital equipment and supplies, and transportation of the patients, supplies and equipment, or the home care staff.

Medical and nursing services were provided in all 31 programs, as were social services. Some form of therapy was provided in 27 of the programs: 11 provided all three—physical, occupational, and speech; 7 provided occupational and physical therapy; one provided physical and speech therapy; one provided occupational therapy only; and 7 provided physical therapy only.

Medicaments and medical supplies were provided in all programs but two. Homemaker service was provided in 28 of the programs, health education in 27, hospital equipment and supplies in 30, and orthopedic appliances in 30 of the programs.

Additional services provided included teaching for home-bound children in three programs, psychological testing in one program, vocational counseling in one program, and provision for transfer of patients in terminal condition to a nursing home in one program serving cancer patients only (table 6).

### Financing

The costs of providing home care were paid for through a variety of sources, which included (1) "allocations drawn from the budget of the administrative agency"; (2) grants given directly to the program from voluntary or philanthropic agencies or organizations, to be used as the administrators of the program saw fit; (3) grants earmarked by the contributing organizations for specific items on the home care budget such as salaries or certain services; (4) payments to the home care programs by welfare departments and other public assistance agencies on behalf of specific patients; (5) services provided and paid for by other community agencies participating in the program, such as visiting nurse services; (6) payments from patients and families for services received; and (7) (notably in those programs administered by public agencies) tax monies allocated from the budget of the political subdivision under which the program operated.

Nine programs were administered by public agencies or institutions. Seven of these were supported primarily by tax funds, either drawn from the budget of the administrative agency or allocated from the total budget of the political subdivision under which the agency operated. In the other two programs, approximately two-thirds of the budget was derived from tax funds, with the remainder being paid through grants from a private foundation. Three of these programs also used services, facilities, space, etc., furnished from other community resources, which were not charged to the home care budget.

In only one of the publicly administered programs did patients defray any of the costs of home care in the year for which data were obtained. This was one of the programs in which patients remained under the care of their private physician if one was available, and patient payments consisted primarily of fees for medical services.

The remaining 22 programs were administered by various private agencies or organizations. In all except one of these programs, endowments and grants from voluntary and philanthropic agencies constituted an important, and in many cases the primary, source of outside funds. The exception was a church-affiliated hospital which provided home care as a charity service to patients and met all costs through the hospital budget. In 11 of the privately administered programs, grams used services, facilities, personnel, etc., from other community resources, provided without charge to the home care budget. In many cases, the monetary value of these services had not been calculated, but, in cases where value was mentioned, the amounts ranged from 5 to 12% of the total costs of home care.

The total costs of the home care programs can be divided into four major categories: (1) costs paid by the home care budget or administrative agency (mon-

TABLE 6.—*Services to Patients and Sources of Services—All Programs**

| | Visiting Physicians | Consultation | Nursing | Social Service | Physical Therapy | Occupational Therapy | Speech Therapy | Health Education | Homemaking | Hospital Equipment | Medicaments and Medical Supplies | Orthopedic Appliances | Transportation of Patients | Transportation of Staff | Transportation of Supplies and Equipment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Alameda County Tuberculosis Home Care Program | C | C | C | H | O | O | O | O | O | H | H&C | H&C | H&C | NS | NS |
| San Francisco Home Care Program | H | H | C | H | H&C | H | C | C | H&C | H&C | H&C | H&C | H&C | H | H |
| University of Colorado General Medical Clinic | H | H | C | H | O | O | O | H&C | C | O | H | H | H | O | O |
| Greater Hartford Home Care Program | C | H&C | C | C | C | C | C | H&C | C | C | O | H&C | C | H&C | H&C |
| D. C. Department of Public Health Home Care Program | H | H | H | H | O | O | O | O | O | H | H | H | H | H | H |
| Georgetown University Home Care Service For Cancer Patients | H | H | H | H | C | C | O | H | H&C | H | H | H | H | H | H |
| Mt. Sinai Hospital Home Medical Care Program | H | O | C | H | C | O | O | H | C | H | H | H | H | H | H |
| Mercy Clinics Home Medical Care Program | H | H | C | H | C | C | O | H | C | C | H&C | C | C | H | H |
| Home Medical Service of Michael Reese Hospital | H | H | C | H | C | C | O | H | C | H&C | H | H | H&C | H | O |
| Chicago Department of Welfare | C | C | C | H | C | O | O | C | H | C | C | C | C | NS | NS |
| Peoria Home Care Program of the V. N. A. | C | C | H | C | H&C | C | C | H | C | H&C | O | C | C | H | H&C |
| Boston Dispensary Home Medical Service | H | H | C | H | C | O | O | H | C | H | H | H | H | H | H |
| Massachusetts Memorial Hospitals Home Medical Service | H | H | C | H | C | O | O | C | C | C | H&C | C | C | NS | NS |
| Department of Home Care, Beth Israel Hospital | H | H | C | H | C | H | O | C | C | H | H | H | H | H | H |
| Home Care Demonstration of Detroit | C | C | H | C | H | H | H&C | H | H | H | H | C | H | H | H |
| St. Mary's Home Nursing Service | C | C | H | C | O | O | O | C | C | H | H | H | C | H | H |
| Home Care Department, Jewish Hospital of St. Louis | H | H | C | H | H | C | O | O | H | H | H | H | H | H | H |
| Mountainside Hospital Extended Care Program | H | H | C | H | H | H | H | C | C | H | H | H | C | H | C |
| New York City Department of Hospitals Home Care Program† | H | H | C | H | C | H | NS | H | H&C | H | H | H&C | H&C | H&C | H&C |
| Montefiore Hospital Home Care Program (New York) | H | H | C | H | H | H | O | C | C | H&C | H | C | H | NS | NS |
| Bronx Hospital Home Care Program for Cancer Patients | H | H | C | H | C | O | C | C | C | H&C | H&C | C | C | O | C |
| Extra-Mural Care Program of The Home for Aged and Infirm Hebrews, New York | C | H | C | H | O | H&C | O | H&C | C | H | H&C | H&C | H | H | H |
| Genesee County Health Department | C | C | H | C | H | O | O | H | O | H&C | C | C | H&C | H | H |
| Home Medical Service, Jewish Hospital of Cincinnati | H | H | C | H | C | O | O | H&C | C | H | H | H | O | H | H |
| The Benjamin Rose Institute | C | C | C | H | C | C | O | O | C | C | C | C | C | O | NS |
| Philadelphia Home Care Program | C | C | H&C | C | H | H | C | H&C | C | H&C | C | H&C | C | H | H&C |
| Montefiore Hospital Home Care Program (Pittsburgh) | H | H | C | H | H&C | C | NS | C | C | H | H | H&C | C | C | H&C |
| Home Care Program of The Albert Einstein Medical Center—Lucien Moss Home—Philadelphia | C | H | C | H | H | H | H | H | H&C | H | H | H | H | H | H |
| University of Vermont Home Care Program | H&C | H&C | H&C | H&C | C | C | C | H | C | C | H | O | C | C | C |
| Richmond, Va., Home Medical Care Program | H&C | H&C | C | H&C | C | O | O | C | C | C | C | C | H&C | H&C | H&C |
| King County (Wash.) Hospital Extension Service | H | H | H&C | H | H | C | C | C | C | H | H | C | H&C | H | H |

* Code: H, facilities and staff of home care program or administrative agency; C, community resources; O, services not provided in program; and NS, source of service not specified.

† Operated in 15 New York City Hospitals—Bellevue, City, Coney Island, Cumberland, Fordham, Goldwater, Gouverneur, Greenpoint, Harlem, Lincoln, Kings County, Metropolitan, Morrisania, Queens General, and Triboro.

patients or their families made some payments for services rendered, but with one or two exceptions these payments were small, and comprised a relatively minor part of the total sources of funds. Some of the programs received some payment from public welfare or assistance agencies on behalf of specific patients. The amount vafied from a very small portion to over approximately one-fourth of the total sources of funds in the various programs. Many of the privately administered programs used here may be allocations from the budget of the administrative agency, grants from private or philanthropic agencies, or tax funds allocated to those programs administered by public agencies); (2) costs paid by public welfare or assistance agencies on behalf of specific patients, and costs paid by public or tax-supported agencies providing services in the program; (3) costs paid by private or voluntary agencies providing services in the program; and (4) costs paid by patients

or families or by private insurance owned by patients. Table 7 shows the sources of payment for direct services to patients, divided according to these four categories, for all programs, and also the sources of payment for salaries of personnel on the home care staff. The total yearly cost of operating the program was not specified in all of the replies, but, where it was, the figures ranged from $2,700 to $95,500.

There did not seem to be any direct relation between the total cost of the program and the number of patients served. For instance, one program which served just over 40 patients during the year cited an approximate total cost of $3,000, while another program with this same case load spent approximately $16,700, more than five times as much. However, certain data that were not obtained in the survey, such as the average number of home visits per patient, or the total number of patient visits, would probably show a more consistent relationship between these two factors, and make possible a more valid comparison of the variations in cost between the different programs.

TABLE 7.—*Sources of Payment, Direct Services to Patients, and Salaries of Home Care Staff Personnel**

| Programs for Which Data Are Available | Home Care Staff Salaries | Visiting Physicians | Consultation | Nursing | Social Service | Physical Therapy | Occupational Therapy | Speech Therapy | Health Education | Homemaking | Hospital Equipment | Medicaments and Medical Supplies | Orthopedic Appliances | Transportation of Patients | Transportation of Staff | Transportation of Supplies and Equipment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Alameda County Tuberculosis Home Care Program | H | H | H | C&W | H | O | O | O | O | O | H | H | O | H | NS | NS |
| San Francisco Home Care Program. | H | H&W | H&W | H,C,W | H | H,C,W | H | H | H | H,C, W,P | H&C | H&C | H&W | H,C,W | H | H |
| University of Colorado General Medical Clinic | H | H | H | C | H | O | O | O | H&C | C | O | H | H | H | C | NS |
| Greater Hartford Home Care Program | H | P&W | P&W | H | C&W | H | H | H | H | H | C,W,P | W,P | H&W | P | H | H&P |
| D. C. Department of Public Health Home Care Program | H | H | H | H | H | O | O | O | O | O | H | H | H | H | H | H |
| Georgetown University Home Care Service for Cancer Patients | H | H | H | H | H | C | C | O | H | H | H | H | H | H&C | H | H |
| Mt. Sinai Hospital Home Medical Care Program | H | H | O | C | H | C | O | O | H | C&W | H | H | H | H | H | H |
| Mercy Clinics Home Medical Care Program | H&C | H&W | H&W | P&C | H | P&W | C,W,P | O | H | P&W | C | H&C | C&W | P&W | H | H |
| Home Medical Service of Michael Reese Hospital | H | H | H | C | H | C | C | O | H | C&W | H&C | H&W | H,W,P | H&W | H | O |
| Peoria Home Care Plan of the V. N. A. | H | P&W | P&W | P,C,W | C&W | P&W | P&W | NS | P | P | P,C,W | O | P,C,W | P&C | H&C | H&C |
| Boston Dispensary Home Medical Service | H | H | H | C&P | H&W | C | O | O | H&W | C&P | H&W | H&W | H&W | P | H | H |
| Massachusetts Memorial Hospitals Home Medical Service | H | H&W | H&W | C | H | C | O | O | C | C | NS | H&C | NS | NS | NS | NS |
| Department of Home Care, Beth Israel Hospital | H | H | H | H | H | H | H | O | H | H&C | H | H | H | H | H | H |
| Home Care Demonstration of Detroit | H | P&W | P&W | P&H | C | H | H | H | P&H | P&H | P&H | P&H | P&W | H&P | H&P | H&P |
| St. Mary's Home Nursing Service.... | H | P&W | P&W | H | P&W | O | O | O | W | C | H | H | H | C | H | H |
| Home Care Department, Jewish Hospital of St. Louis | H | H | H | H | H | H | H | O | O | H | H | H | H | H | H | H |
| New York City Department of Hospitals Home Medical Service† | H | H | H | H | H | H | H | O | H | H&W | H | H | H&W | H | H | H |
| Montefiore Hospital Home Care Program (New York) | H | H | H | H | H | H | H | O | H | H | H | H | H | H | H | H |
| Bronx Hospital Home Care Program for Cancer Patients | H | H | H | H&C | H | C | O | H | C | C&W | H&C | H | H | H | C | H&C |
| Extra-Mural Care Program of The Home for Aged and Infirm Hebrews, New York | H | P&W | H,P,W | H&C | H | O | H&P | O | H,C,P | H,C, P,W | H | H&W | H&W | H | H | H |
| Genesee County Health Department. | H | P&W | H,W,P | H | W | H | O | O | H | O | H&C | P&W | C | H&C | H&C | H&C |
| Home Medical Service, Jewish Hospital of Cincinnati | H | H&P | H | P&C | H | C&P | O | O | C,P,H | W,P,C | H | C,W, H,P | W,H | O | C&P | C&P |
| Philadelphia Home Care Program | H | P,W,H | P,W,H | P,W,H | P&C | C,P,H | P,C,H | P&H | H,C, P,W | P,C,H | W,H, P,C | W,C, H,P | C,P, W,H | H,C,P | H | H&C |
| Montefiore Hospital Home Care Program (Pittsburgh) | H | H | H | H | H | H&C | C | NS | H | H | H | H | C | H | H&C | H&P |
| Home Care Program of The Albert Einstein Medical Center—Lucien Moss Home, Philadelphia | H | P&H | H | H | H | H | H | H | H | H&C | H | H | H | H | H | H |
| University of Vermont Home Care Program | H | H | H | H&C | H,C,W | C | C | C | H | C | C&W | H,W,C | C | W&C | O | H&C |
| Richmond, Va., Home Medical Care Program | H | H | H&W | H | H | H&W | O | O | H | H | H&C | H | H&W | H&W | H | H |
| King County (Wash.) Hospital Extension Service | H | H | H | H | H | H | O | O | O | O | H | H | W&P | W&H | H | H |

* Code: H, costs paid by home care budget or administrative agency; C, costs paid by private or voluntary agencies providing patient services in the program; W, costs paid by public welfare or assistance agencies on behalf of specific patients, or by public or tax-supported agencies providing patient services in the program; P, costs paid by patient, family, or privately-owned health insurance; O, services not provided in program; and NS, source of payment not specified.

† Operated in 15 New York City hospitals.


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## MEDICINE AND THE LAW

*This is the 10th in a series of articles dealing with medical professional liability. An editorial (page 360) and a chronological résumé (page 364) appeared in* THE JOURNAL, *Feb. 2. One of the preceding articles in this series has been published each week in* THE JOURNAL *beginning Feb. 9, 1957, except in the April 13, April 20, April 27, and May 4 issues.*—ED.

# STATE REGULATION OF PROFESSIONAL LIABILITY INSURANCE RATES

Prior to about 10 years ago, there was almost no rate regulation by state insurance supervisory authorities of medical professional liability insurance premiums. In fact, this type of insurance still represents a very small percentage of the total amount of casualty insurance premiums written. As a result of this absence of state regulation, each individual company was at liberty to determine its own rates. However, the National Bureau of Casualty Underwriters assumed jurisdiction in rate promulgation and risk classification on behalf of member insurance companies, effective Sept. 1, 1952. When companies announced that medical professional liability insurance rates were to be increased in some states, many physicians concluded that they were being "taken" and that the announced increases were simply the result of concerted action motivated by selfish interests on the part of the underwriters. Studies have indicated that this was not a justifiable conclusion.

*State Control of Insurance Rates*

| State | Origin of Power: Specific Statutory Authorization | Origin of Power: Implied Statutory Authorization | Exercise of power: Rates Made by Department | Exercise of power: Rates Made by Delegated Authority | Exercise of power: Department Approves or Disapproves Rates Made by Insurer | States in Which Pending or Existing Legislation Relates to Professional Liability Insurance |
|---|---|---|---|---|---|---|
| Alabama | x | | | | x | x |
| Arizona | x | | | | x | x |
| Arkansas | x | x | x | | x | x |
| California | x | x | | | | x |
| Colorado | x | x | | | x | x |
| Connecticut | x | | | | x | |
| Delaware | x | x | | | x | x |
| District of Columbia | x | x | | | x | x |
| Florida | x | x | | | x | x |
| Georgia | x | | | | x | x |
| Idaho | | | | | | x |
| Illinois | x | | | | x | |
| Indiana | | x | | | x | x |
| Iowa | x | | | | x | x |
| Kansas | x | | | | x | |
| Kentucky | x | | | | x | |
| Louisiana | x | | x | | x | x |
| Maine | x | | | | x | |
| Maryland | x | | | | x | x |
| Massachusetts | x | | | | x | x |
| Michigan | x | | | | x | x |
| Minnesota | x | | | x | x | x |
| Mississippi | x | | | | x | x |
| Missouri | x | | | | | x |
| Montana | | | | | | x |
| Nebraska | x | | | | x | x |
| Nevada | x | | | | x | x |
| New Hampshire | x | | | | x | x |
| New Jersey | x | | | | x | x |
| New Mexico | x | | x | | x | x |
| New York | x | | | | x | x |
| North Carolina | x | | | | x | x |
| North Dakota | x | | | | x | x |
| Ohio | x | | | | x | x |
| Oklahoma | x | x | | | x | x |
| Oregon | x | x | | x | x | x |
| Pennsylvania | x | x | | | x | |
| Rhode Island | x | | | | x | x |
| South Carolina | x | | x | | x | x |
| South Dakota | x | x | | x | x | x |
| Tennessee | x | x | | x | x | x |
| Texas | | | | | x | x |
| Utah | x | x | | | x | x |
| Vermont | x | | | | x | x |
| Virginia | x | | | | x | x |
| Washington | | | | | | x |
| West Virginia | x | | x | | x | x |
| Wisconsin | x | x | | | x | x |
| Wyoming | x | | | | x | x |
| Total | 44 | 14 | 5 | 4 | 44 | 43 |

In June of 1945, the Supreme Court of the United States, for the first time, ruled insurance to be interstate commerce and subject to the federal antitrust law. The following year, Congress enacted a measure (P.L. 15, 79th Congress) reaffirming the traditional right of regulation to the states and stipulating that the federal government would assume jurisdiction only to the extent that the business was not regulated by the state supervisory authorities. In addition, P.L. 15 contained a moratorium allowing the states, where necessary, a period of two years in which to adopt statutes that would provide uniform elements of regulation.

As part of a study of medical professional liability, the Council on Medical Service and the Law Department have surveyed the extent to which the several states fix or control insurance rates. The study, which revealed the existence of regulatory laws in almost all of the states, was carried out by means of a questionnaire that was mailed to the insurance departments of the 48 states and the District of Columbia.

The primary purpose of the questionnaire was to determine whether or not there were specific laws on the subject in the respective jurisdictions. A secondary purpose was to learn how the states administered the statutory or implied authority of rate regulation, such as whether the insurance department, by whatever name known, actually fixed rates for all types of casualty insurance or merely exercised control over them by approving or disapproving rate schedules prepared either by the insurance companies or designated rating organizations. A response was received from every state and the District of Columbia, and the results, while not unanimous, were certainly conclusive.

Forty-three states and the District of Columbia indicated that their laws contain specific statutory authority to control or regulate rates for professional liability insurance (see table). Thirteen of the 43 states reported that their laws contain both specific and implied authority. One additional state indicated that its laws contain only implied authority to do so.

Forty-three states and the District of Columbia indicated that their insurance departments did not, themselves or through a delegated authority, fix rates. The respondents stated that they did process and approve or disapprove rates filed by insurers or designated rating organizations, such as: Mutual Insurance Rating Bureau, National Bureau of Casualty Underwriters, and National Insurance Rating Bureau. Nine of these 43 states said that they also fix rates themselves, either by the department directly or through a delegated authority.

# MEDICAL NEWS

## CALIFORNIA

**Los Angeles Art Exhibit.**—The annual exhibition of the Los Angeles Physicians' Art Society will be held May 29-June 28 in the Los Angeles County Medical Association Auditorium. Only paid members may participate and only two pieces may be submitted by an exhibitor. All work must be in by 5 p. m., May 24. A hanging charge of $2.50 will be made for each piece.

Information may be obtained by telephoning Virginia Bown, Executive Secretary, at NOrmandy 3-1062.

**Personal.**—Dr. Robert W. Noyes, assistant professor of obstetrics and gynecology, Stanford University School of Medicine, Stanford University-San Francisco, John and Mary R. Markle Scholar, will spend his sabbatical year doing research at Cambridge University, England.——Dr. J. Joseph Quilligan Jr., associate professor of pediatrics, College of Medical Evangelists School of Medicine, Los Angeles, recently received from the U. S. Army a $13,671 grant for the purpose of studying ways to improve influenza vaccine for children.

## DISTRICT OF COLUMBIA

**Personal.**—Dr. Mario Mollari, chairman of bacteriology and immunology, Georgetown University Medical Center, Washington, D. C., has been elected vice-president of the International Society for the Study of Infectious Diseases, Parasitology, and Immunology.—— Dr. Daniel Leo Finucane has been appointed director of the District of Columbia Health Department, succeeding Dr. Daniel L. Seckinger, who retired Jan. 31. Dr. Finucane has been superintendent and medical director of Glenn Dale Sanatorium since 1939.—— Dr. Basil Blumenthal has been appointed director of the outpatient department at Georgetown University Hospital. Dr. Blumenthal, clinical associate professor of medicine at the university's school of medicine, has been associated with Georgetown since 1947.

**Medical Art on Tour.**—A unique collection of medical art by Rembrandt, Daumier, Hogarth, Toulouse-Lautrec, and other masters was exhibited at the Georgetown University School of Medicine recently. The collection, entitled, "Ars Medica," or the healing arts, was composed of 85 pieces of graphic art depicting the practice of medicine over the centuries. Owned by the Philadelphia Museum of Art, the exhibition is being presented on a cross-country tour by Smith, Kline and French Laboratories, under whose grant the collection was assembled. The scope of the show extends from medical illustrations designed for teaching purposes—such as those of Vesalius, Wechtlin, and others—to portrayals and critiques of medical procedures of the past. Assembled by Carl Zigrosser, curator of prints at the Philadelphia Museum, it is being displayed in mobile units which are especially designed for purposes of the current tour.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

## ILLINOIS

**Dr. Baer Honored.**—Dr. Walter H. Baer, of Peoria, was guest of honor at a testimonial dinner sponsored recently by the Peoria Mental Health Society. His fellow psychiatrists, townsmen, and friends from other parts of the country, gathered to salute Dr. Baer's contributions to mental health in his community, state, and nation, including his work on the Joint Commission on Mental Illness and Health. The principal speaker was Dr. Jack R. Ewalt, director of the joint commission and, like Dr. Baer, one of its founders.

### Chicago

**Cardiac Conference.**—The cardiovascular committee of the Cook County Hospital announces a conference May 21, 11 a. m., at the Children's Amphitheater, 700 S. Wood St. Dr. Aldo A. Luisada, director, department of cardiology, Chicago Medical School, will speak on "Recent Advance in phonocardiography of the Normal and Abnormal Heart." Physicians are invited.

**Personal.**—The directors of the Rehabilitation Institute of Chicago have appointed Dr. Bernard J. Michela as assistant medical director and chief of physical medicine. Since January, 1955, Dr. Michela has been an instructor and consultant in physical medicine and rehabilitation at Georgetown University Hospital and St. Elizabeth's Hospital, Washington, D. C.——Dr. Derrick T. Vail, professor of ophthalmology, Northwestern University Medical School, will be the Doyne Lecturer and Medallist of the Oxford Ophthalmological Congress at Oxford, England, July 1.

## KANSAS

**University News.**—Guest lecturer for the eighth annual student research day at the University of Kansas School of Medicine, Lawrence-Kansas City on May 10 was David Rittenberg, Ph.D., chairman, department of biochemistry, Columbia University College of Physicians and Surgeons, New York City. His subject was "The Evolutionary Development of Enzymes."

## MASSACHUSETTS

**Personal.**—Dr. Henry K. Beecher, Henry Isaiah Dorr professor of research anesthesiology, Harvard Medical School, Boston, was one of five scientists who were sent to Russia by the American Physiological Society. During his travels he lectured before the Academy of Sciences at Leningrad, the Academy of Medical Sciences at Moscow; he also delivered two lectures at Oxford, England, and in Dublin.——A Baird Hastings, Ph.D., Hamilton Kuhn Professor of Biological Chemistry, Harvard University, and head of the department of biochemistry, Harvard Medical School, Boston, has

been named honorary professor on the faculty of medicine,Universidad Nacional Mayor de San Marcos de Lima, Peru. Dr. Hastings received the honor during his participation in a special convocation of the faculty of medicine marking the dedication of the new Institute of Biochemistry and Nutrition at the South American University.——A $29,670 grant from the National Institutes of Health to aid in cancer study was awarded recently to Dr. Shelton C. Sommers, professor of pathology, Boston University School of Medicine, Boston, to be used to study further the effect of human cancer cells upon hamsters.

**State Society Meets in Boston.**—The 176th anniversary of the Massachusetts Medical Society will be celebrated at the annual meeting May 21-23 at the Hotel Statler, Boston. The Shattuck Lecture, "The Patient," will be given by Dr. Leland S. McKittrick, clinical professor of surgery, Harvard Medical School. The Annual Discourse, "Genes, the Heart and Destiny," will be given by Dr. Paul D. White, clinical professor of medicine, Harvard Medical School, who also will be guest speaker at the annual dinner May 22. The following symposiums will be conducted by out-of-state moderators:

Progress in the Treatment of Fractures, with Dr. Preston A. Wade, professor of clinical surgery, Cornell University Medical College, New York City.
Recent Advances in Neurology, with Dr. G. Milton Shy, clinical director, National Institute of Neruological Diseases and Blindness, Bethesda, Md.
Progress in Obstetrics and Gynecology, with Dr. Carl T. Javert, director, obstetrics and gynecology. Woman's Hospital Division, St. Luke's Hospital, New York City.

An art exhibit, an annual golf tournament, and technical exhibits are featured. For information write Dr. Robert W. Buck, Secretary, Massachusetts Medical Society, 22 The Fenway, Boston 15.

## NEW YORK

**Personal.**—Dr. Norvin C. Kiefer, chief medical director of The Equitable Life Assurance Society of the United States, New York City, was chosen president-elect of the National Health Council at its annual meeting in Cincinnati to succeed, in 1958, Mr. Basil O'Connor.

**Society News.**—Officers of the Nassau Radiological Society now include president, Dr. Arthur I. Frucht, Hempstead; vice-president, Dr. Benjamin L. Feuerstein, Bay Shore; treasurer, Dr. John A. Knapp, Hempstead; and secretary, Dr. Jerome Zwanger, Massapequa.

**Surgeons Meet in Lake Placid.**—The International College of Surgeons will hold its New York State sectional meeting at the Whiteface Inn, Lake Placid, N. Y., May 30-June 1. More than 50 surgeons will speak on the scientific program, which will be made up of panel discussions, the presentation of papers, and motion pictures of surgical procedures in color. Dr. James P. Fleming, Rochester, N. Y., is general chairman of the meeting. The following papers will be presented:

Psychiatry in Surgery, Lauchlen S. Palmer, Brooklyn.
Surgical Treatment of Uterine and Vaginal Prolapse, with film in color, Charles H. Thom, Staten Island.
The Acute Abdomen in Pregnancy, Arthur J. Wallingford, Albany.
Reconstructive Surgery, Ross T. McIntire, Chicago.

Dr. Samuel F. Marshall of the Lahey Clinic, Boston, will present a 3-D surgical motion picture in sound and color on "Radical Resection for Carcinoma of the Stomach." Other films in color will be presented by Dr. John E. Dunphy, Boston, and Dr. John G. Mussio, New York. For information write the International College of Surgeons, 1516 Lake Shore Drive, Chicago 10, Ill.

### New York City

**Tuberculosis Conference.**—The annual conference of the New York Tuberculosis and Health Association was held May 14 at the Hotel Statler. The subject of the program, "Tuberculosis and the Homeless Man," was discussed by Dr. Donald J. Ottenberg, Philadelphia; Joan K. Jackson, Ph.D., Seattle; Dr. Anthony Zappala, Washington, D. C.; and Dr. Robert C. Darling, New York City. Speaker at the annual luncheon was Dr. Gardner Middlebrook, director of research and laboratories, National Jewish Hospital, Denver.

**Organize Children's Tumor Clinic.**—A Children's Anemia and Tumor Clinic has been organized at the New York Medical College-Metropolitan Medical Center for the diagnosis, treatment, and special study of problems associated with the chronic hemolytic anemias, leukemia, and malignant diseases of infants and children. The clinics meet on Thursday mornings at Flower and Fifth Avenue Hospitals, 1249 Fifth Ave. (TRafalgar 6-5500 Ext. 237) and Tuesday afternoons at Metropolitan Hospital, 2nd Ave. at 97th St. (ENright 9-6300).

**Nine Million Dollar Medical Gift.**—The Institute of Physical Medicine and Rehabilitation will receive a gift of 9 million dollars from a bequest of the late Louis J. Horowitz, former honorary trustee of the board. According to Dr. Howard A. Rusk, director of the institute, the bequest will be used principally (1) to subsidize patients who cannot otherwise meet the cost of their care, (2) for research, and (3) to establish the first chair of physical medicine and rehabilitation. Before his death, Mr. Horowitz had contributed a total of $1,500,000 to the institute.

**Appoint Chairman of Microbiology Department.**—Alwin M. Pappenheimer Jr., Ph.D., has been appointed professor and chairman of the department of microbiology of New York University College of Medicine to succeed Dr. Colin M. MacLeod, who has become John Herr Musser Professor of research medicine and chairman of the department of research medicine at the University of Pennsylvania School of Medicine, Philadelphia. Dr. Pappenheimer has been on the staff of New York University College of Medicine since 1941 and previously held faculty positions with Harvard and with the University of Pennsylvania. He is editor of the *Journal of Immunology* and *Bacteriological Reviews*, and a member of the Commission on Immunization of the Armed Forces Epidemiological Board.

## OKLAHOMA

**University News.**—The University of Oklahoma School of Medicine, Oklahoma City, has been awarded a $184,000, five-year grant from the National Institute of Mental Health to develop a training program in medical statistics. Dr. Carl R. Doering, professor of preventive medicine and public health, will direct the program.

**Oklahoma Cavalcade of Health.**—The Oklahoma State Medical Association will sponsor a "Cavalcade of Health" at the State's Semi-Centennial Exposition at the Oklahoma City fairgrounds, June 14-July 7. Theme of the exposition will be "Atoms to Arrows," and the Oklahoma State Medical Association's 75 exhibits will illustrate advances in all areas of medical endeavor. A major attraction of the "Cavalcade of Health" will be a manikin, constructed by German scientists and made available by the Dominican Republic's Ministry of Health. The manikin has plastic internal organs which illuminate while the "voice" of the figure explains the function of each.

## SOUTH DAKOTA

**University News.**—Second-year medical students at the University of South Dakota School of Medical Sciences, Vermillion, spend Saturday mornings at the Sioux Valley Hospital, McKennan Hospital, and the Royal C. Johnson Veterans Hospital, where they examine patients under the supervision of the patients' own doctors. The program gives the students their first opportunity to apply basic knowledge in the diagnosis of disease. Working in groups of two or three, the students come in contact with an average of 20 doctors and an equal number of patients during each period. Objective of the program is to help bridge the gap between the student's first two years in the school and work at some other medical school in the student's junior year.

**State Society Meets in Sioux Falls.**—The annual meeting of the South Dakota Medical Association will be held May 18-21 at the Shearton-Cataract Hotel, Sioux Falls. Fourteen papers and two films are scheduled for the four general sessions, with a question and answer hour arranged for the fourth session on "Problems of Peripheral-Vascular Disease" led by Dr. John E. Estes, consultant in internal medicine, Mayo Clinic, Rochester, Minn. The banquet will be held May 20, 7:00 p. m.

The first annual hobby show of the association will open May 19. Association members are invited to make entries of paintings, carvings, collections, etc. For information write the South Dakota State Medical Association, 300 First National Bank Building, Sioux Falls.

## TENNESSEE

**Society News.**—The Tennessee Radiological Society recently elected the following officers: president, Dr. Walter E. Scribner, Kingsport; vice-president, Dr. David S. Carroll, Memphis; secretary-treasurer, Dr. George K. Henshall Jr., Chattanooga. Dr. Herbert C. Francis, Nashville, was nominated counselor to the American College of Radiology and Dr. Walter D. Hankins, Johnson City, was nominated alternate counselor.

**Building Program Completed.**—The University of Tennessee Medical Unit has completed a 5 million dollar building program. The addition of a seventh and eighth floor to the Institute of Pathology Building at a cost of $600,000, will permit the expansion of research and clinical facilities for the College of Medicine's divisions of medicine and surgery. The pharmacy building has been remodeled at a cost of $400,000 and a fifth floor added. This building houses the Division of Pharmacology and the School of Pharmacy. Space also is provided for a laboratory for the U. S. Public Health Service.

**Personal.**—Dr. Kelly Smythe, Bemis, was recently honored by the community he has served for the past 43 years when the seniors of J. B. Young High School dedicated their annual publication to him.—Dr. Phineas J. Sparer, chief of psychiatry and psychosomatics at Veterans Administration Hospital, Memphis, has joined the staff of the University of Tennessee College of Medicine, Memphis, as professor of psychiatry and of preventive medicine. Dr. Sparer is author of a recent book, "Personality, Stress and Tuberculosis."—Dr. Archie R. Foley, who joined the staff of the department of psychiatry, University of Tennessee College of Medicine, Memphis, in 1955, has accepted a year's appointment at the Institute of Neurology, Queen Square, University of London.—Dr. Ralph F. Morton, instructor in medicine, University of Tennessee College of Medicine, Memphis, has been awarded the C. Riley Houck Investigatorship established by the Tennessee Heart Association. The award carries a stipend of $7,200 for the first year. It was established in memory of the late associate professor of physiology at the medical units, who was doing research work in diseases of the heart and blood vessels when he died of a heart attack. Dr. Morton also has been awarded the Frank W. Dugan Fellowship in Cardiology, established by the widow of the late Memphis lumberman.

## HAWAII

**Society News.**—The Honolulu Pediatric Society recently elected the following officers to serve during 1957: president, Dr. William A. Myers; recording secretary, Dr. Allan C. Oglesby; and corresponding secretary-treasurer, Dr. Clifford K. Kobayashi, all of Honolulu.

## GENERAL

**Obstetrics and Gynecology Certification.**—The American Board of Obstetrics and Gynecology announces that applications for certification, new and reopened, for the 1958 part I examinations are now being accepted. Deadline date for receipt of applications is Sept. 1. Current bulletins outlining present requirements may be obtained by writing to Dr. Robert L. Faulkner, American Board of Obstetrics and Gynecology, 2103 Adelbert Rd., Cleveland 6, Ohio.

**Dominican Republic Malaria Fund.**—A check for $100,000 was given recently to Dr. Fred L. Soper, director, Pan-American Sanitary Bureau, regional office of the World Health Organization, Washington, D. C., by the Ambassador of the Dominican Republic to the United States, His Excellency Joaquin E. Salazar. This money is the first installment of a $500,000 contribution of the Dominican Government for the special fund for malaria eradication of the Pan-American Sanitary Organization. It is the second contribution to the fund, the first, in the amount of $1,500,000, having been made in March by the government of the United States.

**Physical Medicine Prize Lecture.**—To stimulate interest in physical medicine and rehabilitation, the American Congress of Physical Medicine and Rehabilitation will award annually a prize for an essay. Among the rules which apply to the contest are: Manuscripts MUST BE in the office of the American Congress of Physical Medicine and Rehabilitation, 30 N. Michigan Ave., Chicago 2, not later than June 1. An original and one carbon copy of each manuscript not exceeding 3,000 words must be submitted. The winner will receive $200, a gold medal, a certificate of award, and an invitation to present the contribution before the annual session of the American Congress of Physical Medicine and Rehabilitation in Los Angeles, Sept. 8-13.

**Investigative Dermatology Meeting.**—The 18th annual meeting of the Society for Investigative Dermatology, Inc., will be held at the Belmont Plaza, New York City, June 1-2. Among the speakers on the program are George C. Wells, St. Thomas Hospital University of London, who will present "On the Origin of the Free Fatty Acids of Human Surface Fat," and Drs. Edwin Sidi, Marc Hincky, and Robert Longueville, Paris, France, who will present "Cross-Sensitization Between Neomycin and Streptomycin." A cocktail party and dinner ($10 a person) will be held June 1, 7 p.m. Dr. Harry L. Arnold Jr., of Honolulu, will be the speaker of the evening. For information write Dr. Herman Beerman, Secretary-Treasurer, 255 S. 17th St., Philadelphia 3.

**Meeting on Air Pollution Control.**—The Air Pollution Control Association will celebrate its golden anniversary June 2-6 at a meeting at the Jefferson Hotel, St. Louis, Mo., in which celebration the American Meteorological Society, the American Institute of Chemical Engineers, the American Society of Mechanical Engineers and the American Society of Heating and Air Conditioning Engineers will join in the celebration. This will be the first time these five organizations will unite their efforts for a program devoted solely to air pollution and its control. At this meeting each society will develop information related to its special field of technological interest. The address of the executive secretary of the Air Pollution Control Association is Harry C. Ballman, 4400 Fifth Ave., Pittsburgh 13, Pa.

**Free Cardiac Surgery Program.**—National Jewish Hospital at Denver in expanding its cardiovascular program, will consider applications of patients suffering from cardiovascular defects amenable to surgical intervention, including mitral and aortic stenosis, congenital cardiac anomalies. Definitive diagnosis is not necessary prior to admission, inasmuch as the hospital has a completely equipped cardiopulmonary physiology laboratory. Patients are accepted without regard to race, religion, or national origin, and without charge. Only those unable to pay for private care are eligible. Periodic reports are made routinely to the referring physician. Inquiries should be sent to Medical Director, National Jewish Hospital, Denver 6, Colo.

**Research Conference on Food and Nutrition.**—The 1957 Gordon Research Conference on Food and Nutrition will be held at Colby Junior College for Women, New London, N. H., Aug. 19-23. These conferences were established to stimulate research, and this purpose is achieved by an informal type of meeting consisting of lectures and free discussion groups. The program does not aim to review known fields of nutrition and food technology but to bring experts up to date on the latest developments and to provoke suggestions for making further progress. No publications are prepared as emanating from these conferences. Attendance is limited to 100. Persons interested in attending may address Wilber George Parks, Ph.D., Director, Department of Chemistry, University of Rhode Island, Kingston, R. I.

**Physicians Invited to German Parley.**—The German Foreign Office recently invited a group of American public health workers to be guests of the German Government for a four-week tour of the Federal Republic of Germany. Round-table discussions with representatives of federal ministries were scheduled so that the guests might present their own particular problems and learn how similar problems are dealt with in Germany. The tour is part of an exchange program with the United States inaugurated in 1952. The group included Dr. Eugene F. Lutterbeck, president of the German Medical Society of Chicago; Dr. Raymond Frank Barnes, American National Red Cross, St. Louis; Dr. Robert Dyar, California State Department of Public Health, Berkeley, Calif.; Dr. Henry A. Holle, State Department of Health, Austin, Texas; and Miss Margaret McLaughlin, Public Health Service, Charlottesville, Va.

**Hospitalized Children.**—One out of every 14 boys and one out of every 17 girls under age 20 are hospitalized in the course of a year, the Metropolitan Life Insurance Company's statisticians report on the basis of the experience among dependent children of the company's personnel. The study, concerning claims involving at least one night of hospital stay, showed that the average length of hospital stay was 5½ days. Youngsters 5 through 9 years of age had the shortest stay, averaging not much over 3 days. This is accounted for largely by the fact that tonsillectomies, which constituted the bulk of the cases at these ages, averaged only slightly more than one day in the hospital. The 15 through 19 age group had the longest average stay—about 9 days. Two-thirds of the hospitalized cases had

surgery. Duration of the hospital stay was much shorter for the surgery cases than for the nonsurgical, averaging less than half as long.

**Scholarship for Study Abroad.**—The Committee on Medical Education of the New York Academy of Medicine will award one scholarship grant in the amount of $4,700 for the academic year 1958-1959 to provide aid for advanced study abroad in a clinical subject in preparation for the practice of medicine or surgery. Candidates must be male interns or residents in voluntary, municipal, or Veterans Administration hospitals in New York City. The course of study, the auspices under which it is to be taken, and the place or places where the study is to be pursued must receive the approval of the committee, which stipulates that the study be pursued abroad, preferably in Great Britain or in continental Europe. Applications must be submitted by Sept. 1. Information may be obtained by writing to Dr. Robert L. Craig, Executive Secretary, Committee on Medical Education, New York Academy of Medicine, 2 E. 103 St., New York 29.

**Nuclear Institute Traveling Lecture Program.**—The National Science Foundation recently announced a grant of $115,800 to the Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn., to carry out its expanded Traveling Science Demonstration Lecture Program for 1957-1958. Sponsored by the foundation in cooperation with the U. S. Atomic Energy Commission, which is contributing $38,000, the "traveling teacher" program is designed to stimulate interest in science and science-teaching careers on the part of secondary-school students. Announcements about the program are being sent to 30,000 high schools throughout the United States. Information concerning the program and brochures announcing the 1957-1958 activity can be obtained by writing Oak Ridge Traveling Science Demonstration Lecture Program, University Relations Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn.

**Angiologists Meet in New York.**—The annual meeting of the American College of Angiology will be held at the Plaza Hotel, New York City June 1-2. A symposium on cardiac surgery will be held June 1 with Dr. Frank Glenn, Lewis Atterbury Stimson Professor of Surgery, Cornell University Medical College, New York, as moderator. A symposium on peripheral vascular disease will be moderated by Dr. Alvin A. Bakst, clinical assistant professor of surgery, State University of New York College of Medicine, Brooklyn. Dr. E. Jefferson Browder, professor, department of neurosurgery, State University of New York College of Medicine, Brooklyn, will serve as moderator of a panel discussion on vascular disease of the brain, to be held June 2. Scientists interested in vascular medicine are invited. For information write Dr. Anafred N. Halpern, Secretary, American College of Angiology, 15 E. 62nd St., New York 21, N. Y.

**Therapeutic Society Meets in New York.**—The 58th annual meeting of the American Therapeutic Society will be held May 30-June 2 at the Essex House, New York City. The scientific program includes the following symposiums: Newer Aspects of Therapy in Hematology, moderated by Dr. Paul Reznikoff, clinical professor of medicine, Cornell University Medical College, New York City; Newer Aspects of Antibiotics; and Management of Hypertension, moderated by Dr. George A. Perera, associate professor of medicine, Columbia University College of Physicians and Surgeons, New York City. Dr. Robert W. Wilkins, president-elect, American Heart Association, and professor of medicine, Boston University School of Medicine, will speak on "From Snake Root to Serotonin" at the presentation of the third Oscar B. Hunter Memorial Award in Therapeutics. Further information may be obtained from Dr. Oscar B. Hunter Jr., Secretary, American Therapeutic Society, 915-19th St. N. W., Washington 6, D. C.

**Annual Report on Accidents.**—The National Safety Council announces that in 1956 accidents killed 95,000 persons in the United States, injured 9,450,000, and cost $10,800,000,000. Despite a 2% increase in accidental deaths over the 1955 figure, the population death rate went down slightly—from 56.9 to 56.8—because of a relatively greater increase in population. Motor vehicle accidents remained the nation's No. 1 accident killer, with a 4% increase; home accidents claimed the second largest number of lives (27,500); and accidents at work (14,300), the third. Deaths from falls numbered 20,000 in 1956; from burns, 6,800; from drownings, 5,900; and from firearms, 2,150. Catastrophes in which the toll was at least 5 lives occurred less frequently in 1956 (1,300) than in 1955 (1,150). Only one catastrophe in 1956 caused more than 50 deaths—the June 30 collision of two passenger planes over the Grand Canyon in Arizona, in which 128 persons were killed. In February a military plane crash in California cost 40 lives, and in July another military plane crash in New Jersey killed 46. Two other catastrophes brought death tolls of 25 and 30 persons.

**Society News.**—Officers of the **American Association of Medical Clinics** now include: Dr. G. Gordon McHardy, Browne-McHardy Clinic, New Orleans, president; Dr. George Plain, The South Bend Clinic, South Bend, Ind., vice-president; and Dr. Harold D. Caylor, Caylor-Nickel Clinic, Bluffton, Ind., secretary-treasurer.——At the annual meeting of the **North Pacific Society of Neurology Psychiatry** the following officers were elected: president, Dr. Douglas E. Alcorn, Victoria, B. C.; president-elect, Dr. John W. Evans, Portland, Ore.; secretary-treasurer, Dr. Robert M. Rankin, Seattle.——At the recent meeting of the **American Dermatological Association** the following officers were elected: president, Dr. Clark W. Finnerud, Chicago; vice-president, Dr. Hamilton Montgomery, Rochester, Minn.; secretary, Dr. J. Lamar Callaway, Durham, N. C.; treasurer, Dr. Carl T. Nelson, New York City.——The **American Society for Artificial Internal Organs** elected the following officers at a recent Chicago meeting: president, Dr. Peter F. Salisbury, Los Angeles; president-elect, Dr. George H. A. Clowes Jr., Cleveland; secretary-treasurer, Dr. George E. Schreiner,

Washington, D. C.; and council members, Drs. William J. Kolff, Cleveland; Clarence Dennis, Brooklyn; Robert Bowman, Bethesda, Md.

**Award in Neurological Surgery.**—The American Academy of Neurological Surgery announces its third annual award given for the best paper submitted reporting original clinical or laboratory research pertaining to the nervous system for which the author has had the primary responsibility. Eligibility is confined to doctors of medicine currently training in neurological surgery or those who have completed training since June 30, 1955, except those who have been certified by the American Board of Neurological Surgery or by the Royal College of Surgeons of Canada, subspecialty neurosurgery. The recipient will present his paper at the 19th annual meeting of the American Academy of Neurological Surgery at The Cloister, Sea Island, Ga., Nov. 11-13. His expenses while attending the meeting and his travel expenses to and from his home (if living outside the North American Continent, from the port of entry into the United States) will be borne by the academy, and there will be an honorarium of $100. Manuscripts should be sent to Dr. Eben Alexander Jr., Secretary to the Academy, at the Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C., before July 15. A resume of the candidate's postdoctoral training must accompany the paper when submitted.

**Meeting in New York on Sterility.**—The American Society for the Study of Sterility will hold its 13th annual meeting at the Waldorf-Astoria Hotel, New York City, May 31-June 2. A demonstration of methods and research in treatment of sterility in leading institutions has been arranged by Dr. Alan F. Guttmacher, clinical professor of obstetrics and gynecology, Columbia University College of Physicians and Surgeons, New York City, and Dr. Charles M. McLane, assistant professor of obstetrics and gynecology, Cornell University Medical College, New York City. A special address, "A Society Comes of Age," will be given by Dr. Wesley T. Pommerenke, of Rochester, president of the society. A round-table discussion, "Endometriosis and Sterility" and a luncheon panel discussion, "Therapeutic Irradiation," moderated by Dr. C. Lee Buxton, professor of obstetrics and gynecology, Yale University School of Medicine, New Haven, Conn., are scheduled. A breakfast round-table discussion will be conducted June 2. The program includes the following topics and speakers:

Diagnosis and Treatment of Sterility in the Male, with Especial Reference to Sperm Motility, Robert S. Hotchkiss, professor of urology, New York University Postgraduate Medical School, New York City.

Endometrium and Sterility, Arthur T. Hertig, Shattuck Professor of Pathological Anatomy, Harvard Medical School, Boston.

Psychogenic Sterility, Robert A. Cleghorn, professor of psychiatry, McGill University, and Carlo G. Bos, senior staff, department of psychiatry, McGill University, Montreal, Canada.

The 1957 Ayerst Lecture, "Laboratory and Clinic in the Study of Infertility," will be given by Dr. George W. Corner, Rockefeller Institute, New York City.

## EXAMINATIONS AND LICENSURE

AMERICAN BOARD OF ANESTHESIOLOGY: *Part I.* Various locations, July 19. Final date for filing application was Jan. 19. American Board of Anesthesiology. *Oral.* Washington, Oct. 28-Nov. 1. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY: *Written.* Several cities, June 27. *Oral.* Baltimore, Oct. 11-13. Final date for filing application was April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 21. *Oral.* Los Angeles, Sept. 11-14. Final date for filing applications was Feb. 1. Exec. Sec., Dr. W. A. Werrell, 1 West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Applications for certification, new and reopened, for the 1958 Part I examinations are now being accepted. Deadline for receipt of applications is September 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Chicago, Oct. 7-11. *Written.* January 1958. Final date for filing application is July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland 9, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* New York City, Jan. 29-31, 1958. Final date for filing application is August 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 7-11. Final date for filing application was in April. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written. Pathologic Anatomy and Clinical Pathology.* New Orleans, Sept. 26-28. Final date for filing application is August 15. Sec., Dr. Edward B. Smith, Indiana University Medical Center, Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Oral.* San Francisco, June 21-23. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Parts I and II.* New York City, June 8-9. Final date for filing application was March 1. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written. Parts I and II.* September. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 16-17. San Francisco, March 17-18. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: Washington, Sept. 23-28. Final date for filing application is June 1. Within the near future a special examination for certification in Nuclear Medicine will be offered to diplomates in Radiology and Therapeutic Radiology. Sec., Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part II.* New York, June 10-11. Sec., Dr. John B. Flick, 225 S. 15th St., Philadelphia 2.

AMERICAN BOARD OF UROLOGY: *Written examination.* Various cities throughout the country. *Pathology and Oral Clinical.* February 1958. Location not decided. Exec. Secretary, Mrs. Ruby L. Griggs, 30 Westwood Road, Minneapolis 16.

BOARD OF THORACIC SURGERY: *Written.* Various centers throughout the country, September 1957, and the closing date for registration is July 1, 1957. Sec., Dr. William H. Tuttle, 1151 Taylor Ave., Detroit 2.

# DEATHS

Mahoney, **John Friend,** medical director, U. S. Public Health Service, retired, New York City; born in Fond du Lac, Wis., Aug. 1, 1889; Marquette University School of Medicine, Milwaukee, 1914; specialist certified by the American Board of Preventive Medicine; commissioned a medical officer in the Public Health Service in 1917; later spent four years in Haiti, Ireland, England, and Germany, where he did research on venereal diseases; then became director of the venereal disease research laboratory of the U. S. Marine Hospital, now the U. S. Public Health Service Hospital, on Staten Island, a position he held for 20 years; formerly health commissioner of New York City; director of the bureau of laboratories of the New York City Health Department, a post he held at the time of his death; service member of the American Medical Association; in 1946 won the Lasker Award of the American Public Health Association for research into the penicillin treatment of syphilis; also received awards from the Association of Military Surgeons of the United States, the American Social Hygiene Association, the National Association of Venerealogists of Mexico, and the National Federation of Medicine in Guatamala; served as chairman of the Committee of Experts on Venereal Disease of the World Health Organization; chairman of the National Advisory Serology Council and of the Committee on Standardization of Serological Tests for Syphilis of the American Public Health Association; at one time associate clinical professor of dermatology and syphilology at New York University College of Medicine and in dermatology at Columbia University College of Physicians and Surgeons; author of articles, published in professional journals; died in the U. S. Public Health Service Hospital, Stapleton, L. I., Feb. 23, aged 67, of cerebral hemorrhage.

**Napier, Charles Dwight,** Sag Harbor, N. Y.; born in Brooklyn Jan. 31, 1864; Columbia University College of Physicians and Surgeons, New York City, 1890; served on the faculty of the Long Island College of Medicine; an associate member of the American Medical Association; member of the American Orthopaedic Association and the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; formerly practiced in Brooklyn, where he was attending orthopedic surgeon, House of St. Giles the Cripple, and on the staffs of St. Mary's, Kings County, Methodist, St. John's Episcopal, Caledonian, Long Island College, and Wyckoff Heights hospitals, and the Southampton (N. Y.) Hospital; died Feb. 18, aged 93, of myocardial failure.

**Dyment, Bertha Sabin Stuart,** Stanford, Calif.; born in Memphis, Mich., July 18, 1878; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1908; served with the Red Cross overseas during World War I; in 1934 resigned as medical adviser to women and director of physical education for women at Stanford University, Palo Alto, which she joined in 1929; assistant director of physical education for women at her alma mater from 1902 to 1907, when she became director; served as director of physical education for women and medical adviser at the University of Oregon, Eugene, and the Reed College in Portland, Ore.; formerly associated with the California State Board of Health; died Feb. 1, aged 78.

**Leydic, Clarence Loraine,** Tarentum, Pa.; born March 30, 1872; Western Pennsylvania Medical College, Pittsburgh, 1897; an associate member of the American Medical Association; veteran of World War I; for many years examining physician for the school district; during World War II and the Korean conflict was medical officer for the district draft board and was awarded certificates of meritorious service by presidents Roosevelt and Truman; one of the founders of the Allegheny Valley Hospital, where he served as a member of the staff; chairman of the board of the First National Bank in Tarentum; surgeon for the Pennsylvania Railroad; died Feb. 3, aged 84, of coronary occlusion.

**Albertson, Harvey S.,** Oswego, N. Y.; born in 1875; Cleveland Homeopathic Medical College, 1907; an associate member of the American Medical Association; veteran of World War I; became Oswego city health officer in 1920 and continued in that office until 1930; one of the founders of the Oswego County Health Association and for many years vice-president; served as trustee of the Oswego City Savings Bank; member of the board of managers of Oswego County Sanatorium in Richland; an emeritus member of the staff and formerly member of the division of pathology at the Oswego Hospital, where he died Feb. 7, aged 81, of coronary sclerosis.

**Fortescue, Thomas Aloysius,** Captain, U. S. Navy, retired, Paoli, Pa.; born in Philadelphia Sept. 23, 1884; Jefferson Medical College of Philadelphia, 1908; interned at the Philadelphia General Hospital; appointed an assistant surgeon in the medical corps of the U. S. Navy Aug. 29, 1913; during his more than 33 years active service served with the Navy Medical Department throughout the United States and on board ships of the fleet; placed on the retired list by reason of physical disability on May 1, 1947; service member of the American Medical Association; died in the U. S. Naval Hospital, Philadelphia, Feb. 22, aged 72, of myocardial infarction.

**Jackson, Walter Leo** ✱ High Point, N. C.; born in Reidsville, Nov. 1, 1884; North Carolina Medical College, Charlotte, 1911; past-chairman of the High Point Civil Service Commission; a member of the board of directors of the State Medical Care Commission; formerly associated with the Guilford General Hospital; past-president of the medical staff of High Point Memorial Hospital; past-president and

✱ Indicates Member of the American Medical Association.

member of the board of directors of the local YMCA; past-president of the Kiwanis Club; vice-president and member of the board of directors of the Central Savings Bank; died Jan. 26, aged 72, of coronary thrombosis.

**Pattison, Harry Archibald,** Claverack, N. Y.; born in 1877; Chicago Homeopathic Medical College, 1904; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1910; fellow of the American College of Physicians; member of the American Trudeau Society, British Tuberculosis Association, and the International Union Against Tuberculosis; served as supervisor of the medical service of the National Tuberculosis Association; formerly director of the Potts Memorial Institute in Livingston; author of "Rehabilitation of the Tuberculous"; died in the Columbia Memorial Hospital, Hudson, Feb. 14, aged 79, of cerebral hemorrhage.

**Reisinger, John Charles** ✦ Washington, D. C.; born in Rockville, Md., Aug. 23, 1901; George Washington University School of Medicine, Washington, D. C., 1927; specialist certified by the American Board of Internal Medicine; medical adviser to the district branch of the Selective Service System; instructor of medicine at Johns Hopkins University School of Medicine, Baltimore, from 1930 to 1931, when he became clinical instructor of medicine at George Washington University School of Medicine, serving until 1935; formerly on the staff of the Central Dispensary and Emergency Hospital; died in the George Washington Hospital March 5, aged 55.

**Wiedenmann, John Charles** ✦ Englewood, Colo.; born in Hepler, Kan., June 14, 1899; Johns Hopkins University School of Medicine, Baltimore, 1930; served as secretary and president of the Arapahoe County Medical Society; for many years county health officer and city physician; one of the founders and past-president of the Englewood Rotary Club; a director of the Denver Chapter of Arthritis and Rheumatism Foundation; served on the staffs of Swedish National Sanatorium in Englewood, and St. Luke's Hospital and the Porter Sanitarium and Hospital in Denver, where he died Jan. 12, aged 57, of cerebral hemorrhage.

**Eisenstein, Victor William** ✦ New York City; born Sept. 15, 1904; George Washington University School of Medicine, Washington, D. C., 1929; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychosomatic Society; fellow of the American Psychiatric Association; served a residency at the New York State Psychiatric Institute and Hospital in New York City; chief in psychiatry at the Lenox Hill Hospital; editor of "Neurotic Interaction in Marriage" and the author of articles in the scientific journals; died Feb. 3, aged 52, of coronary disease.

**Foley, Floyd K.** ✦ Owensboro, Ky.; born March 29, 1885; University of Louisville (Ky.) Medical Department, 1911; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; past-president of the Kentucky Psychiatric Association; veteran of World War I; formerly superintendent of the Eastern State Hospital in Lexington and the Western State Hospital in Hopkinsville; at one time with the Pension Bureau in Washington, D. C.; died in the Veterans Administration Hospital, Louisville, Feb. 3, aged 71, of myocardial infarction.

**Mecray, Paul Mulford,** Camden, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1892; member of the founders group of the American Board of Surgery; veteran of the Spanish-American War; for many years secretary of the Camden County Medical Society; fellow of the American College of Surgeons; retired chief of staff, Cooper Hospital, where he was a member of the board of managers; served on the staff of the Salem (N. J.) County Memorial Hospital and the Zurbrugg Memorial Hospital, Riverside; died in Lake Wales, Fla., Feb. 13, aged 85, of coronary occlusion.

**Joelson, James Joel** ✦ Cleveland; Columbia University College of Physicians and Surgeons, New York City, 1920; clinical professor of urology at the Western Reserve University School of Medicine; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; veteran of World War II; associate surgeon in charge of genitourinary surgery, University Hospitals of Cleveland; died in the Hanna House of University Hospitals Feb. 8, aged 59, of coronary thrombosis.

**Howe, Hubert Shattuck** ✦ New York City; Columbia University College of Physicians and Surgeons, New York City, 1912; specialist certified by the American Board of Psychiatry and Neurology; member of the American Neurological Association and the Association for Research in Nervous and Mental Diseases; for many years clinical professor of neurology at his alma mater; served on the staffs of the Presbyterian Hospital and the Neurological Institute; died in the Roosevelt Hospital Feb. 4, aged 68.

**Maresh, Henry Rudolph** ✦ Houston, Texas; University of Texas School of Medicine, Galveston, 1919; formerly clinical assistant professor of clinical medicine at the Baylor University College of Medicine; member of the staffs of St. Joseph's and Methodist hospitals; on the visiting staff of Hermann Hospital; a consultant in internal medicine at Polly Ryon Memorial Hospital, Richmond; died in the M. D. Anderson Hospital Jan. 28, aged 66, of bronchogenic carcinoma with metastases.

**Aday, J. Leo** ✦ Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1937; fellow of the American College of Surgeons; veteran of World War II; on the staffs of the St. Vincent Infirmary and the Arkansas Baptist Hospital, where he died Feb. 15, aged 44, of coronary thrombosis.

**Becker, William Christian,** Winter Park, Fla.; Jefferson Medical College of Philadelphia, 1917; service member of the American Medical Association; at one time an officer in the regular Navy; retired from the Veterans Administration on March 28, 1956; died Feb. 19, aged 67.

Comer, **Robert T.** ✱ Birmingham, Ala.; Johns Hopkins University School of Medicine, Baltimore, 1901; for many years head of the health department of the Avondale Mills; died March 4, aged 80, of ascending kidney infection and benign prostatic obstruction.

Dozier, **William Bate** ✱ Nashville, Tenn.; University of Nashville Medical Department, 1905; member of the American Academy of General Practice; died in the Mid-State Baptist Hospital Jan. 27, aged 74, of pneumonia.

Eichenbronner, **David,** Amsterdam, N. Y.; Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg, Baden, Germany, 1902; an associate member of the American Medical Association; on the staffs of the Amsterdam City Hospital and St. Mary's Hospital, where he died Jan. 25, aged 78, of arteriosclerotic coronary artery disease.

Ernst, **Harold Oliver,** New Orleans; Tulane University School of Medicine, New Orleans, 1922; member of the Louisiana State Medical Society; died in the Touro Infirmary Nov. 26, aged 57, of bronchogenic carcinoma of the right lung.

Farquhar, **Elwood Miller,** Santa Monica, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1897; died Jan. 17, aged 88.

Fisher, **Leon Gabriel,** New York City; Columbia University College of Physicians and Surgeons, New York City, 1912; medical examiner for the New York State Department of Labor; died in the Maimonides Hospital, Brooklyn, Feb. 3, aged 66, of ruptured aortic aneurysm.

Forbes, **Stephen Alfred** ✱ Chicago; Rush Medical College, Chicago, 1937; assistant professor of radiology at the University of Illinois College of Medicine; at one time assistant professor of radiology at the State University of Iowa College of Medicine in Iowa City; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; died March 16, aged 47.

Fuesy, **Joseph Ralph,** Croton-on-Hudson, N. Y.; New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1953; interned at Grasslands Hospital in Valhalla; certified by the National Board of Medical Examiners; served a residency at the White Plains (N. Y.) Hospital and St. Luke's Hospital in New York City, where he died Jan. 31, aged 32, of leukemia.

Garding, **Clarence Jacob,** Jefferson, Wis.; Creighton University School of Medicine, Omaha, 1927; veteran of World War I; on the staffs of the Fort Atkinson (Wis.) Memorial Hospital and the St. Mary's Hospital in Watertown, where he died Jan. 25, aged 57, of polycystic kidney.

Gerwitz, **Bernard William** ✱ St. Louis; St. Louis University School of Medicine, 1930; instructor in gynecology and obstetrics at his alma mater; member of St. Louis Medical Society and St. Louis Gynecological Society; since 1933 assistant gynecologist and obstetrician at St. Mary's Group of Hospitals; formerly on the staff of St. Louis City Hospital; died Jan. 29, aged 53, of cancer.

Gilstrap, **William J.,** ✱ Portland, Ore.; College of Physicians and Surgeons of San Francisco, 1903; died in the Grande Ronde Hospital, La Grande, Feb. 12, aged 86, of carcinoma of the colon with metastases.

Givens, **Robert T.,** New Castle, Va.; University College of Medicine, Richmond, 1901; died in the Lewis Gale Hospital, Roanoke, Dec. 23, aged 80.

Goldstein, **David,** Brooklyn; Long Island College Hospital, Brooklyn, 1906; died Jan. 3, aged 72, of arteriosclerotic heart disease.

Graves, **Allen Bouthrod,** New York City; Howard University College of Medicine, Washington, D. C., 1908; died Feb. 3, aged 78, of cerebral arteriosclerosis.

Greenberg, **Samuel** ✱ Newark, N. J.; University and Bellevue Hospital Medical College, New York City, 1904; on the staff of the Beth Israel Hospital, where he died Feb. 8, aged 75, of cerebral hemorrhage.

Gregory, **Dewey Quintin** ✱ Eureka, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1943; interned at the Los Angeles County Hospital, in Los Angeles; killed in an automobile accident Feb. 3, aged 58.

Gruskin, **Harry** ✱ Brooklyn; Boston University School of Medicine, 1928; veteran of World War II; died in the Mount Sinai Hospital, New York City, Jan. 14, aged 52, of diabetes mellitus, cirrhosis of the liver, and nephrosis.

Guy, **Franklin Wheeler,** New Castle, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1906; an associate member of the American Medical Association; on the staff of the Jameson Memorial Hospital; died Feb. 6, aged 86, of cerebral hemorrhage.

Hall, **Samuel J.,** ✱ Medical Director, U. S. Public Health Service, Philadelphia; University of Louisville (Ky.) School of Medicine, 1927; died Feb. 1, aged 57, of coronary occlusion.

Hamilton, **Robert Lucian** ✱ Marysville, Calif.; University of Tennessee College of Medicine, Memphis, 1929; member of the American Academy of General Practice; fellow of the International College of Surgeons; veteran of World War II; decorated with the Purple Heart and received the Army Commendation Ribbon; past-president of the Yuba-Sutter-Colusa Counties Medical Society; died Feb. 1, aged 52, of coronary occlusion.

Haney, **Frederick Charles** ✱ Watertown, Wis.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1907; died in St. Mary's Hospital Dec. 9, aged 77, of lymphosarcoma and pneumonia.

Harris, **Carl Nathaniel** ✱ Hibbing, Minn.; Rush Medical College, Chicago, 1915; past-president of the Minnesota State Sanitary Association; veteran of World War I; village health officer from 1934 to 1942; on the staff of the Adams Clinic and Hibbing General Hospital; died in the Methodist Hospital, Rochester, Minn., Feb. 10, aged 69, of carcinoma of the lung.

**Hayes, Floyd Warner** ✱ Bradford, Pa.; University of Buffalo School of Medicine, 1914; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; veteran of World War I; an honorary member of the staff of the Bradford Hospital, where he died Feb. 9, aged 67, of cerebral hemorrhage.

**Heath, Guy Wilkerson,** West Palm Beach, Fla.; Tulane University School of Medicine, New Orleans, 1920; member of the Florida Medical Association; member of the staff of St. Mary's Hospital, where he was on the advisory board, and the Good Samaritan Hospital; died in Jupiter Feb. 3, aged 62, as the result of a boat accident while fishing in the ocean.

**Heberding, John** ✱ Youngstown, Ohio; Western Pennsylvania Medical College, Pittsburgh, 1905; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society and the American College of Radiology; on the staff of the Youngstown Hospital; died Jan. 26, aged 74, of cancer.

**Hildebrant, Paul Wiley,** Mount Sterling, Ohio; University of Michigan Homeopathic Medical School, Ann Arbor, 1912; formerly mayor; died in Washington C. H., Jan. 30, aged 80.

**Hollings, Byam** ✱ Concord, N. H.; Harvard Medical School, Boston, 1906; in 1914 member of the House of Delegates of the American Medical Association; member of the Massachusetts Medical Society; veteran of World War I; retired assistant medical director for the John Hancock Life Insurance Company in Boston; died Jan. 25, aged 79, of cerebral vascular accident.

**Hopkins, Howard Leslie** ✱ Leavenworth, Wash.; University of Nebraska College of Medicine, Omaha, 1928; veteran of World War II; died Feb. 17, aged 55.

**Horwitz, John B.** ✱ Detroit; Detroit College of Medicine and Surgery, 1926; veteran of World War II; member of the American Academy of General Practice; on the staffs of Grace and Sinai hospitals; died Jan. 13, aged 55, of coronary occlusion.

**Hughes, Fred Morris** ✱ Houston, Texas; University of Texas School of Medicine, Galveston, 1926; veteran of World War I and II; at one time associate professor of clinical surgery at Baylor University College of Medicine; on the staffs of the Memorial, Hermann, and St. Luke's hospitals; on the courtesy staff of St. Joseph's Hospital, where he died Jan. 28, aged 58, in the operating room after completing a minor operation on a patient.

**Hull, Austin Oliver** ✱ San Antonio, Texas; University of Louisville (Ky.) Medical Department, 1913; for many years city bacteriologist; died in Santa Rosa Hospital Jan. 28, aged 65, of thrombosis.

**Hunter, John Russell Wightman,** Lewistown, Pa.; Medico-Chirurgical College of Philadelphia, 1893; an associate member of the American Medical Association; fellow of the American College of Surgeons; member of the surgical staff and board of trustees for many years at the Lewistown Hospital, where he died Jan. 26, aged 88, of cerebral thrombosis.

**Hutchinson, Sankey Smith,** Bladenboro, N. C.; North Carolina Medical College, Charlotte, 1911; member of the Medical Society of the State of North Carolina; served as past-president of the Bladen County Medical Society; chairman of the city and county board of education; surgeon for the Scotland Air Line Railway; on the staff of the Robeson County Memorial Hospital, Lumberton, where he died Feb. 11, aged 68, of myocardial infarction.

**Jacobs, William Rigby** ✱ Lewiston, Idaho; Rush Medical College, Chicago, 1937; specialist certified by the American Board of Ophthalmology; veteran of World War II, receiving the Air Medal with three oak leaf clusters; chairman of the ophthalmological section, St. Joseph's Hospital; died Jan. 26, aged 50, probably of coronary thrombosis.

**Jamieson, William Ross** ✱ El Paso, Texas; McGill University Faculty of Medicine, Montreal, Quebec, Canada, 1898; also a graduate in pharmacy; past-president of the El Paso County Medical Society; veteran of World War I; on the staff of the El Paso General Hospital and the Hotel Dieu, Sisters' Hospital; died in the Veterans Administration Hospital, Fort Bayard, N. Mex., Jan. 24, aged 81.

**Jamison, Euell Claude** ✱ Rocky Mount, Va.; Medical College of Virginia, Richmond, 1927; veteran of World War II; member of the Roanoke Academy of Medicine; member of the Rocky Mount Town Council; a director of the Bankers Trust Company of Rocky Mount; trustee of the Franklin Memorial Hospital, where he was an active member of the medical staff; died Jan. 29, aged 56, of lymphosarcoma.

**Johnston, Irwin,** Cohoes, N. Y.; Albany (N. Y.) Medical College, 1911; an associate member of the American Medical Association; served on the staff of the Samaritan Hospital in Troy; died Feb. 13, aged 70, of arteriosclerotic heart disease.

**Jones, J. N.,** Bastrop, La.; Memphis (Tenn.) Hospital Medical College, 1907; member of the Louisiana State Medical Society; died in the Bastrop General Hospital Nov. 29, aged 76, of congestive heart disease.

**Kazlauckas, Anthony John** ✱ Cleveland; St. Louis University School of Medicine, 1931; formerly Cuyahoga County deputy coroner; on the staff of the Polyclinic Hospital, where he died Jan. 18, aged 52, of cerebral hemorrhage.

**Landis, James Calvin,** Pennsburg, Pa.; Medico-Chirurgical College of Philadelphia, 1902; for many years member of the school board; served on the staff of the Quakertown (Pa.) Community Hospital, where he died Feb. 10, aged 79.

**Lanning, Walter Benjamin,** De Queen, Ark.; University of Arkansas School of Medicine, Little Rock, 1913; died Feb. 7, aged 72, of aneurysm of the aorta.

**Latta, Reginald Heber,** Graysville, Ohio; Ohio State University College of Medicine, Columbus, 1917; member of the Ohio State Medical Association; mayor of Graysville and president of the Monroe County Board of Health; died Jan. 18, aged 64, of coronary thrombosis.

**Lauter, Leo** ✦ Toledo, Ohio; Albertus-Universität Medizinische Fakultät, Königsberg, Prussia, Germany, 1920; member of the American Academy of General Practice; on the staffs of the St. Luke's and Flower hospitals; died Feb. 11, aged 63.

**Leaper, Warren Eugene** ✦ Green Bay, Wis.; Johns Hopkins University School of Medicine, Baltimore, 1911, past-president of the Brown-Door-Kewaunee Counties Medical Society; on the staffs of St. Vincent's, Bellin Memorial, and St. Mary's hospitals; died Jan. 20, aged 70, of coronary occlusion.

**Leavitt, Thomas William,** Malden, Mass.; College of Physicians and Surgeons, Boston, 1920; member of the Massachusetts Medical Society; veteran of World War I; formerly Malden alderman; died in Medford Feb. 6, aged 65.

**Lemon, Charles Warner,** Lewisburg, W. Va.; University College of Medicine, Richmond, 1898; an associate member of the American Medical Association; in 1914-1915 member of the state legislature; staff physician at Greenbrier Military School from 1932 until 1955; died in the Greenbrier Valley Hospital, Ronceverte, March 6, aged 81.

**Leonard, John Vaughn,** Menlo Park, Calif.; Medical Department of the University of California, San Francisco, 1901; died in the Palo Alto (Calif.) Hospital Jan. 28, aged 79.

**Lessig, James Blee** ✦ Sinking Spring, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1930; on the staff of the Reading (Pa.) Hospital, where he died Jan. 23, aged 51, of carcinoma of the lung.

**MacFarlane, Nowland,** Pacific Palisades, Calif.; Beaumont Hospital Medical College, St. Louis, 1900; formerly practiced in Los Angeles, where he was on the staffs of the Clara Barton, Queen of Angels, and Methodist hospitals; died Jan. 26, aged 80.

**McEwan, James William,** Alma, Mich.; L.R.C.P., Edinburgh and L.R.C.S., Edinburgh, Scotland, 1904; Detroit College of Medicine, 1907; veteran of the Spanish-American War and World War I; formerly practiced in Detroit, where he was on the staff of the Harper Hospital; died Jan. 23, aged 80, of carcinoma of the rectum.

**McLean, Harold Guy** ✦ Detroit; Detroit College of Medicine and Surgery, 1920; fellow of the International College of Surgeons and the American College of Surgeons; vice-chief of surgery at the Grace Hospital, where he died Feb. 8, aged 60, of coronary occlusion.

**McWilliams, Jacob Marvin** ✦ Fayetteville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1901; died in the Lincoln County Hospital Feb. 2, aged 79, of cerebral hemorrhage.

**Mars, John Francis,** Newburgh, N. Y.; McGill University Faculty of Medicine, Montreal, Quebec, Canada, 1918; member of the Medical Society of the State of New York; served on the staff of the Cornwall (N. Y.) Hospital; on the courtesy staffs of Goshen (N. Y.) Hospital and St. Luke's Hospital; died Jan. 26, aged 64.

**Max, Clarence Oscar Christian** ✦ St. Louis; Washington University School of Medicine, St. Louis, 1899; served on the staffs of St. Mary's Hospital, St. Mary's Infirmary, St. Anthony Hospital, and Missouri Baptist Hospital; died in Barnes Hospital Feb. 15, aged 82, of myocardial infarction.

**Mayo, Bessie Evelyn,** Oklahoma City, Okla.; Baylor University College of Medicine, Dallas, Texas, 1923; died Jan. 20, aged 58, of rheumatic heart disease.

**Mellies, George Augustus** ✦ St. Louis; Homeopathic Medical College of Missouri, St. Louis, 1895; member of the American Academy of General Practice; veteran of World War I; for many years associated with the Christian Hospital, where he was for many years chief surgeon and president of the medical staff, and where he died Feb. 1, aged 82, of heart disease.

**Mellman, Clarence,** Los Angeles; College of Physicians and Surgeons, Los Angeles, 1917; died Jan. 29, aged 62, of acute cardiac failure.

**Messerly, Charles Buchanan** ✦ Martins Ferry, Ohio; College of Physicians and Surgeons, Baltimore, 1902; for many years served on the board of education of Martins Ferry; at one time county coroner; veteran of World War I; a director of the Citizens Savings Bank; one of the founders of the Martins Ferry Hospital, where he was a member of the staff, and where he died Jan. 31, aged 77, of coronary disease.

**Moore, Russell Malachi** ✦ Atlanta, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1885; died Jan. 21, aged 93, of carcinoma of the lungs.

**Morris, Harry Rembert** ✦ Birmingham, Ala.; University of Nashville (Tenn.) Medical Department, 1906; died in Miami, Fla., Feb. 13, aged 73, of pulmonary edema, portal cirrhosis, and portal-vein thrombosis.

**Murray, Robert Allen** ✦ La Mesa, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1938; certified by the National Board of Medical Examiners; served on the staffs of Mercy and Quintard hospitals in San Diego; died Jan. 17, aged 47, of squamous-cell carcinoma of the tongue and floor of mouth.

**Myers, Lloyd** ✦ San Diego, Calif.; University of Nebraska College of Medicine, Omaha, 1918; died Dec. 21, aged 65, of hypertensive cardiovascular heart disease.

**Owen, John Atkinson,** South Boston, Va.; University of Virginia Department of Medicine, Charlottesville, 1903; died in the Veterans Administration Hospital, Richmond, Jan. 24, aged 76, of arteriosclerosis.

**Pantera, George Benedict** ✦ Buffalo; Georgetown University School of Medicine, Washington, D. C., 1936; certified by the National Board of Medical Examiners; formerly practiced in Oak Hill, where he was on the staff of the Oak Hill Hospital; died in Cleveland Feb. 8, aged 47, of heart disease.

**Parmenter, Bert Newton,** Sheboygan, Wis.; Northwestern University Medical School, Chicago, 1896; died in the Sheboygan Memorial Hospital Feb. 26, aged 86, of auricular fibrillation, and coronary sclerosis.

# FOREIGN LETTERS

## INDIA

**Basal Cell Carcinoma.**—M. V. Sirsat (*Indian J. M. Sc.* 11:1, 1957) compared the age, incidence, site of occurrence, and histopathology of basal cell carcinoma in Indians and Europeans. Between 1941 and 1955, 200 cases of basal cell carcinoma were recorded in the laboratories of the Tata Memorial Hospital, Bombay, of which 148 occurred in Indians and 52 in Europeans. Most of these patients were between 41 and 60 years of age. There was no significant difference in age distribution in the two groups. The most frequent sites of occurrence of the tumor in Indians were the cheek, eyelids, and nose, while in Europeans the most frequent site was the nose. The reticulated variety of basal cell carcinoma was commonest in Europeans and the adenoid cystic type in Indians.

**Shortage of Nurses.**—At the meeting of the Central Council of Health at Ranchi, there was deep concern over the limited progress made in implementing the recommendations of the nursing committee. Therefore, the council again urged state governments to improve the emoluments and working conditions of nurses. About 17,000 nurses and 21,000 midwives are practicing in India. This number falls far short of the needs. The health survey and development committee had recommended that there should be a ratio of one nurse to every 500 persons and one midwife for every 100 births. On this basis, the total requirements of nurses and midwives would be 70,000 and 87,500 respectively. In order to meet the increasing demand for health personnel, a plan for training about 6,000 additional auxiliary-nurse midwives has been included in the second Five-Year Plan.

**Lymphomas of the Pharynx.**—G. V. Talwalkar (*J. Postgraduate Med.* 3:1, 1957) studied 54 cases of malignant lymphoma of the pharynx, which constituted 10% of the proved malignant lymphomas encountered in a period of 15 years. The patients varied in age from 6 to 85 years, 35 being between 30 and 60. The duration of symptoms varied from eight days to one year, the most usual time being two to three months. Swelling of the neck was the main complaint in 20 cases. Generalized enlargement of lymph nodes was present in three patients. Pain in the throat was a common complaint. Difficulty in swallowing was present in 13 patients; a mass in the throat in 11; a change in voice in 5; and epistaxis in 4. Deafness was the only complaint in one. The tonsils were primarily involved in 35 patients. Of these, 10 showed an ulcerative lesion, 5 showed a bulky growth, 6 showed uniform enlargement of the tonsils, and 9 had a nodular growth. Most nasopharyngeal lymphomas were large and occupied most of the nasopharyngeal space. Lesions seen at the base of the tongue were either ulcerative or nodular. Lymph nodes were palpable in 45 cases. Most of the patients underwent irradiation therapy, three after tonsillectomy. Complete regression of the primary lesion and the cervical lymph nodes was seen within two months in 24 patients. Partial response was noticed in 12. One patient with generalized lymphosarcoma with a lesion in the tonsil responded well to nitrogen mustard. A complete follow-up was not available, as patients failed to return. Histologically, follicular lymphoma was diagnosed in two patients, both in the tonsils.

**Nystatin in the Treatment of Moniliasis.**—Pohowalla and co-workers (*Indian J. M. Sc.* 11:1, 1957) stated that, since thrush is commonly seen in children, they sought to assess the effectiveness of nystatin in its treatment. Twenty-eight children with thrush were studied clinically and 27 of these also bacteriologically. The disease was clinically cured in 75% of the patients by the seventh day of treatment. Cultures became negative in 60% of the children within the same period. The nystatin was given orally. Diarrhea was the commonest complication of thrush, being present in 75% of the patients; 13 of these patients also showed dehydration. All the seven deaths that occurred in the series were in dehydrated patients.

**Isolated Fracture of the First Rib.**—Donaldson and Marshall (*Indian Journal of Surgery,* December, 1956) reported a case of isolated fracture of the first rib. This condition is so infrequently encountered that it is apt to be missed. This is due to the situation of the first rib deep in the base of the neck, where it is usually protected from trauma by the shoulder girdle. The importance of this fracture lies in the fact that it may result in rupture of the apex of the lung, abscess formation, pleurisy with effusion, hemorrhage, nerve pressure and Horner's syndrome. The authors' patient was a 54-year-old man who, while lifting baggage, had felt a sudden excruciating pain in the left upper portion of his chest. This was followed by breathlessness and faintness. These symptoms were relieved by nikethamide and coffee. The pain persisted but was ignored by the patient till about six weeks later when he started getting pain in the left side of his neck, left shoulder, and arm. The pain increased in severity and radiated down to the tips of his middle and ring fingers. He also complained of a feeling of something filling the left upper portion of his chest. A roentgenogram showed fracture of the left first rib at the costochondral junction.

## NEW ZEALAND

**Synaptic Transmission in Sympathetic Ganglions.**—At the 32nd meeting of the Australian and New Zealand Association for the Advancement of Science, in Dunedin, in January, Rosamond M. Eccles of the Australian National University, Canberra, reported that when the synaptic transmission of impulses through the isolated superior cervical ganglion was blocked by

The items in these letters are contributed by regular correspondents in the various foreign countries.

curare-like substances, preganglionic impulses still produced three types of postganglionic potentials: a synaptic potential, a later positive potential (P wave), and a late negativity (LN) wave superimposed on the latter part of the P wave. Addition of any anticholinesterase, in a suitable concentration, causes a complete disappearance of the LN wave, and thereby reveals the full size and time course of the P wave. This effect of anticholinesterases is due to their anticholinesterase action and not to any depolarization of the postsynaptic membrane, since depolarizing agents such as nicotine or increased potassium ion concentration do not selectively decrease the LN wave. Other pharmacological agents such as epinephrine, strychnine, and veratrine do not cause any appreciable alteration in the size or time courses of the synaptic potentials, the positivity wave, or the late negativity wave. Such results indicate that synaptic transmission in the sympathetic ganglion is more complicated than at the neuromuscular junction, where only a single transmitter appears to be operating on a single type of membrane receptor.

**Bloat.**—Bloat is a disorder of ruminants that occurs wherever grazing of legumes is practiced. It is the result of interference with elimination of gas that is normally produced by the bacterial fermentation of food in the rumen and reticulum. At the same meeting, A. T. Johns and co-workers of Palmerston North reported the results of trials undertaken to test the various theories put forward to explain the cause of the ailment. It was found that most of the gas produced was being retained in a foam and therefore not free to be eructated. A system of control of bloat caused by leguminous pastures was evolved, using vegetable oils as antifoaming agents. The tendency of certain animals to bloat appears to be an inherited characteristic, and, hence, both pasture and animal factors seem to be involved. Trials with the use of orally administered penicillin to protect animals from bloat indicate that the flora of the rumen is a major contributing factor.

**Endocrine Adaptations to the Tropics.**—At the same meeting, Prof. W. V. Macfarlane of Brisbane stated that metabolic rate and thyroid activity have been found to be depressed in rats, sheep, and man by periods of living at temperatures above 30 C. Food intake is reduced and water intake increased. The metabolically active components of the adrenal steroid secretion also appear to be depressed during the hot seasons and elevated during the cooler parts of the year. This applies to 17-ketosteroid output and 17-hydroxycorticoid excretion. The intake of water by man and sheep in summer is increased to about 12 times the winter intake. When evaporative cooling is employed in the hotter parts of the year, antidiuretic hormone appears in the blood to reduce urine flow. Urine flow, however, is reduced at these times without there being measurable amounts of antidiuretic hormone in the blood. The antidiuretic hormone appears to be an adjuvant to other water-saving mechanisms. It is released by heat (four hours at 41 C) in summer, but not in winter, in man and sheep.

In both species, the ratio of potassium to sodium in the urine is high in summer and low in winter. This is associated with aldosterone excretion after sweat-producing exercise such as that described by Neher and Wettstein. It was found that the potassium/sodium ratio in the urine becomes high within two hours of exposure to a temperature of 40 C. As this ratio rises, the antidiuretic hormone concentration in the blood also rises. Artificial acclimatization of sheep by the use of 0.15 mg. of desoxycorticosterone acetate per kilogram of body weight intramuscularly did not produce antidiuretic hormone at rest in a neutral environment (22 C), but, on heating, these animals were found to have high levels of antidiuretic hormone in the plasma. This action lasts for about one day, and after that, heat, again, in winter produces no antidiuretic hormone. It appears that the salt-saving hormones, which appear earlier than antidiuretic hormone in the hot season, prepare the cells by increasing intracellular sodium and decreasing the intracellular water so that there is a more facile release of water-saving hormone.

In the northern parts of Australia there is a 30% reduction in conception during summer as compared to winter. Comparison of data from towns of similar population in the north and south of the country showed lower reproductive rates in man in the hot region than in the cooler parts of the south. Among sheep and cattle in the tropical regions there is a low rate of reproduction. In the tropical pasture lands, conception rarely occurs in more than 60% of the ewes and cows. In rats and rabbits, it has been found that large numbers of fetuses resorb if the animal is maintained at a temperature of about 35 C. Analysis of this fetal resorption has shown that supplementary thyroid hormone, increased protein and vitamin intake, or supplementary progesterone can save a certain number of fetuses from resorption. Acclimatization, however, appears to be the most satisfactory means of protecting the fetus even though the number of ovulations is reduced by acclimatization for one month at 35 C. The protection afforded by acclimatization is completely overcome by injections of 2 mg. a day of cortisone. It appears that excessive mobilization of cortisone or 17-hydroxycorticosterone may account for fetal resorption. Such resorption has been observed in sheep also, and it may be that the human fetus may be resorbed in the early stages of gestation if the mother is exposed to high ambient temperatures. Temperatures up to 43 C occur in the summer in the Australian tropics.

**Hypophysectomy in Man.**—At the same meeting, Dr. J. A. James and co-workers of the Neurosurgical Unit of the Dunedin Hospital reported a series of 21 patients with disseminated mammary cancer who were subjected to hypophysectomy. There were three operative deaths. Two patients with cancers arising during pregnancy were not influenced by the procedure. Several patients were followed up for only a short time, but two patients survived for over a year. There is often great relief from pain in those with bony metastases. Cutaneous deposits tend to heal. There is

a differential effect whereby skin metastases may be held in check while lymphatic and visceral deposits progress. The ability of the kidney to retain water is reduced. The patients are easily maintained on cortisone and thyroid therapy. The pituitaries were put into fixative immediately after removal. The histological appearances were without the usual features of postmortem autolysis. Special staining methods have been used to confirm the presence of three different types of basophilic cells whose postulated function concerns the thyroid gland and gonads. So far, the preoperative endocrine status has thrown no light on the identity of the different types of basophilic cells. In some patients the urinary sodium/potassium ion ratio was not diminished after operation. Where this ratio was affected, the fall was gradual and not sudden. Aldosterone was assayed in the urine before and after hypophysectomy in some patients. It was found that aldosterone production persists, at least partly, after hypophysectomy, and this finding is interpreted as indirect evidence that the stimulus to augmented aldosterone production after surgical trauma is a circulating tropic hormone elaborated by the diencephalon. This center would be functionally or anatomically damaged during removal of the pituitary.

**Brucellosis.**—At the same meeting, Dr. M. M. Wilson of the University of Melbourne reported a steady rise in the incidence of brucellosis since 1937 in Victoria, Australia. From 1950 to 1955, inclusive, official reports in all states revealed that more than half the cases occurring in Australia were in Victoria, and that in all states except South Australia fewer cases were reported from the capital than from the rest of the state. Brucellosis in man is almost invariably acquired from animals or animal products. In Victoria, the organism concerned is the bovine species, Brucella abortus. There are no accurate figures on the incidence of contagious abortion in cattle, but there is no doubt that large quantities of infected milk are still being drunk, particularly in rural areas. Few infections, however, seem to be contracted in this way. The preponderant incidence of brucellosis is among those who handle cattle, such as dairy farmers, veterinarians, and meat-workers. This suggests that the spillover of infection from the bovine reservoir to man is by direct manual contact. Another important source is strain 19, which is sometimes accidentally autoinoculated during its administration to cattle. This attenuated strain can produce clinical brucellosis in man. From the experience in Victoria it is clear that brucellosis should be considered in many a clinical problem and that the antiglobulin test is a useful procedure in support of the standard agglutination test. Repeated attempts at culture should also be made.

**Leptospirosis.**—At the same meeting, Dr. E. H. Derrick of Brisbane, Queensland, stated that the causative organism in more than 350 cases of leptospirosis studied belonged to 13 serotypes, the commonest being Leptospira australis A and Leptospira australis B. The identity of the animal carrier was established in only five cases. All but 11 patients were male. The ages ranged from 5 to 68 years. About 55% worked in sugar cane fields; other groups included schoolboys, timbergetters, scrub clearers, bridge and tramway workers, and miners. Most cases came from the high-rainfall coastal strip where the annual rainfall exceeds 90 inches, but sporadic cases occurred in drier regions. Most cases occurred in the wet season (January to April). Outbreaks also occurred during the canecutting season (June to December). The incidence was high in the vicinity of rivers and creeks and on wet lowlying canefields. There were no deaths. In two patients uremia and in one jaundice developed. The average duration of fever was five days; it tended to be longer with L. australis B infections. The prognosis is much better than formerly in Queensland. When the average duration was 10 days, 16% became jaundiced and 5% died. The improvement is due partly to the greater inclusion of milder types but mainly to the introduction of penicillin therapy. Penicillin is effective if given early and in a dosage of 2.5 to 4 mega units daily. Prevention is largely an unsolved problem. Control measures include the burning of cane before cutting, the use of adequate footwear, drainage of wet fields, and anti-rat campaigns.

**Antileptospiral Effect of Milk.**—At the same meeting, Dr. L. Kirschner and co-workers of Otago University, Dunedin, said that it had been reported that Leptospira rapidly died in milk from cows, goats, and human beings, and it was concluded that the presence of this antileptospiral agent in cow's milk explained the absence of milk-borne infections in the many countries in which bovine leptospirosis is endemic. Studies have been made using the electron microscope to check the disintegration of Leptospira at various intervals after mixture with milk and to compare it with the lytic effect exerted by immune serums and 1% sodium desoxycholate. After an interval of 45 minutes the beginning of the destruction of one of the components of the Leptospira (the protoplasmic cylinder) is clearly demonstrated. The effect is much more marked after 3 hours, and after 12 to 40 hours only the resistant second component of the structure of the organisms, the axial filament, surrounded by protoplasmic masses, is visible. The organisms are similarly affected by 1% sodium desoxycholate. The effect of lytic antibodies in human and rabbit immune serums is quite different. After a transient agglutination the Leptospira are transformed into spherical shining particles, with complete loss of structure.

## UNITED KINGDOM

**Health of Colored Immigrants.**—Figures on the health of colored immigrants in West Bromwich, Birmingham, were given by Dr. Skone. Last year there were 838 in the area of a total population of 88,000. About 60% were West Indians, the remainder being Indians and Pakistanis. As immigrants from the Commonwealth, provided they were not aliens, they were not subject to a detailed medical examination on arrival in Great Britain. A local survey of their health, however, was made. The incidence of tuberculosis was 2%, or more than four times that in the country as a whole.

Colored patients comprised the majority of those seen at the local venereal disease clinics in 1955 and 1956. West Indians comprised the majority of those with gonorrhea. An increasing number of patients with granuloma inguinale, a disease rarely encountered except at a few of the ports, were seen. One Indian had leprosy.

**Unemployment Pay for Physicians.**—It would have been unthinkable a few years ago that physicians might draw unemployment pay. Under the welfare state they are entitled to do so. Most of those availing themselves of this source of income are temporarily unemployed, usually hospital residents or interns who may have to wait weeks or months for a suitable appointment. The day is gone when a physician could fill in such time as a locum tenens in a private practice. There is no reason why the physician, having paid in compulsory insurance against unemployment, should not obtain the benefits claimed by the rest of the community. Certain senior members of the profession, however, disapprove of this attitude, and the dean of one medical school refuses testimonials to any physician who has drawn unemployment pay.

**Empire Rheumatism Council.**—To celebrate its 21st birthday, the Empire Rheumatism Council has launched an appeal for $700,000 for research into rheumatism. The appeal, which is under the direction of Lord Astor, is directed mainly toward industry. The council states that rheumatic diseases account for 10% of all working days lost through illness. They account for more absenteeism from work than do industrial disputes. About 27.5 million days a year are lost to industry through rheumatic illness and about 2 million from strikes. This is more than for tuberculosis and bronchitis, which together result in a loss of 25.5 million working days, and industrial accidents, which are responsible for 16 million days lost. All these figures are minimal as absences due to illness of less than four days are not recorded.

**Prescribing Proprietary Drugs.**—In an effort to cut down the mounting drug bill, the Ministry of Health is trying to dissuade physicians from prescribing proprietary drugs, which are often but not always more expensive than the corresponding pharmacopeial preparations. Many physicians agree in principle but consider that proprietary drugs often have some advantages in practice over the official preparations. This is borne out by the investigations of Bagnall and Stock, who subjected 343 samples of barbiturate tablets to tests laid down by the British Pharmacopeia (*Pharm. J.* 177:441, 1957). They found that 79 of the 343 samples, or 23%, failed to conform to pharmacopeial standards. This figure included drugs issued both under proprietary and official titles. Bagnall and Stock also showed that there are marked differences between the tablets of different manufacturers. Many pharmaceutical manufacturers spend large sums on research. Some firms with low standards do not and are thus able to undersell their competitors, sometimes with inferior products sold as pharmacopeial preparations. *Lancet* takes the view that if a physician is convinced that certain proprietary preparations are better than those supplied as official equivalents, he has every right to prescribe the former if he wishes to.

**Mass Radiography of Refugees.**—Mass miniature radiography of several hundred Hungarian refugees has shown that they have a higher incidence of pulmonary tuberculosis than is general in Great Britain. The Ministry of Health has, therefore, asked health officers to offer mass radiography to those refugees who are still in camps or hostels or who are working together in sufficiently large numbers to justify the visit of a mobile radiography unit. Refugees working in isolated areas will also be asked to visit a mass radiography center. The examination is, however, purely voluntary.

**Micrococcic Diarrhea.**—Cook and co-workers (*Brit. M. J.* 1:542, 1957) reported that 31 cases of diarrhea following antibiotic therapy occurred in the Radcliffe Infirmary, Oxford. Fourteen of the patients died, most of the deaths occurring in patients who had a partial gastrectomy. Some deaths occurred in medical patients who had had prolonged courses of antibiotics, mainly for respiratory infections. Micrococcus pyogenes var. aureus was isolated from the stools of 20 of the patients, and it was considered that the indiscriminate prophylactic use of penicillin and streptomycin in combination was the chief predisposing cause of the diarrhea. A strain of M. pyogenes var. aureus resistant to the antibiotics in use at the time presumably established itself in the usually sterile small intestine and dominated the complex and usually stable flora of the colon. The routine use of antibiotics in abdominal surgery and chronic medical conditions in condemned. The authors recommend that their use should be restricted to patients with a special indication, such as a perforation or soiled peritoneal cavity at operation, and that the patient should be kept isolated. Otherwise the improper use of antibiotics may lead to tragedy. It is considered that the sufonamides can be used in most cases for the preparation of patients for abdominal operation. In conjunction with such measures, attempts should be made to reduce the number of M. pyogenes var. aureus in the patient's environment, not only to avoid sepsis but also to allow the safe and effective use of antibiotics when they are needed. Since the restriction on their use at the Radcliffe Infirmary in the last six months, there has been no severe case of micrococcic diarrhea. Even the use of the newer antibiotics is no guarantee against this.

**Complications of Measles.**—Most children obtain no benefit from routine sulfonamide prophylaxis as regards measles, according to a report on the complication of measles (*Research Newsletter* no. 14, p. 51, Feb., 1957). The proportion of severe cases was high (8 or 9%) among patients aged between 6 months and 2 years. It then fell to about 6%, this rate persisting until the age of 7 years. Thereafter it rose again, reaching 15% in the 11-to-15-year age group and about 30% among patients over 15 years of age. The proportion of cases classified as severe was significantly higher among girls (8.4%) than among boys (6.2%). The pro-

portion of severe cases among all children under 7 years of age was consistently higher in patients with chronic sinusitis than in those without the disorder. Of the 2,338 children under 5 years of age in the investigation, 1,184 were mainly breast-fed. Over the whole five-year period the incidence of mild cases was 36.4% of breast-fed patients and 29.7% of bottle-fed patients—a statistically significant difference. It could not be shown that a history of measles in the mother had any additional effect on the protection given by breast feeding. For all breast-fed patients under 5 years of age, the percentage of mild attacks among children whose mothers had had measles was lower (36%) than among those whose mothers had not had measles (40%).

The report concludes that the routine use of sulfonamides in the early stages of measles does not uniformly lower the incidence of complications. It lowers the rate for acute otitis media in older children and in those with chronic sinusitis, and it is especially valuable in those with a past history of otitis media. On the other hand, it does nothing to reduce the rate of severe pulmonary complications and may be a factor in raising this rate, especially in children under 2 years of age or in others with a mild attack. In other words, there is no evidence to suggest that either sulfonamides or antibiotics are of prophylactic rather than curative value.

**Doctor or Mister.**—A protest against the traditional British custom of referring to a surgeon as "Mister" and not "Doctor" is registered in a scholarly article by Dr. George Graham (*Lancet* 1:264, 1957), who says that this curious practice, which does not exist in any other country, seems to arise from the old antagonism between the Royal College of Physicians and the Barber Surgeons Company after its formation in 1540. The members of the company rarely, if ever, had a degree of doctor of medicine, and their general education was certainly inferior to that of the physicians. Furthermore, in those days the surgeons were under the domination of the physicians. Now that the standards for physicians and surgeons are the same, it is strange that the distinction should still exist. This practice causes much confusion among patients and the general public who cannot understand why a properly qualified doctor should not be so called. It also causes inconvenience to themselves if they travel in countries where all medical men are called "Doctor."

**Portacaval Anastomosis.**—In the *Lancet* (Jan. 12, 1957) R. M. Walker states that the indications for portacaval anastomosis are hemorrhage from esophageal and gastric varices resulting from intrahepatic venous obstruction and the risk of such hemorrhage when large varices are known to exist. Contraindications to the operation are the presence of severely impaired liver function and a portal vein unsuitable for anastomosis. To determine the site of venous obstruction, transsplenic portal venography is used as a routine procedure. Of a series of 56 patients, on each of whom end-to-side portacaval anastomosis was performed, 53 survived the operation. In each of the 50 of those who had not had a previous portal venous system operation, there was no recurrence of the hemorrhage. The most serious drawback of the operation was neuropathy, which may complicate a portal venous shunt. Transient symptoms were the usual complication, occurring in 20% of the patients and ranging from mental disorientation to coma, and could be precipitated by taking a large protein meal. In most patients there was no evidence of deterioration of liver function during the follow-up period, which in some cases was five years. Thus, portacaval anastomosis has an important place in the management of portal hypertension.

**The Elderly Disabled.**—Many older persons admitted to the hospital have nowhere to go on discharge. Yet many have some degree of disability; thus they are forced to stay in the hospital. Their beds are urgently needed, and the cost of keeping these patients hospitalized is from $33 to $43 a week. The administrative gap between the National Health Service and the National Assistance Act is responsible for this situation. Since World War II a great deal had been done for older people, including the setting up of 70 geriatric units and 900 residential homes. The home-nursing service made 12.5 million visits a year to the elderly. A survey made on behalf of the Ministry of Health led to the conclusion that, if greater coordination of the efforts of hospitals, physicians, and welfare officers with welfare and local authorities could be made, more efficient use of the available services would ensue. Thus, by additional home help, a number of hospitalized patients might return home, releasing much-needed beds.

**Recurrent Goiter.**—Piercy and Lange (*Lancet*, Jan. 26, 1957) report that of 3,500 patients seen at the thyroid clinic, 118 had true recurrence of goiter or thyrotoxicosis after thyroidectomy had been performed. Several were found to be in a hypothyroid state with hypertrophied remnants of gland due to stimulation by thyrotropic hormone. These patients were treated successfully by thyroid extract. The treatment of recurrent goiter is difficult, and radioactive iodine has a useful place in the regimen, but, even so, only 17 of the true recurrences were treated with it. Its main use has been in patients with associated vocal cord disorders in whom tetany was a complication of the operation and in whom cardiovascular involvement contraindicated operation. Many so-called recurrences are the continued growth of adenomatous tissue left behind from an earlier operation. The authors recommend inspection of the entire gland at the first operation. The inferior thyroid arteries should always be ligated, as this is a potent factor in preventing recurrence. The ligations are carried out in continuity, the artery being found by deliberately exposing the carotid artery. At operation, any pyramidal lobe and all obviously pathological tissue must be removed. If the remnants left behind consist of healthy secretory thyroid tissue, sufficient thyroid hormone for the body will be produced; if the remnant is only the compressed rim of the thyroid gland, all will be well. The authors believe that most recurrences are preventable.

# CORRESPONDENCE

## AMERICAN ACADEMY OF PEDIATRICS AS POISON FIGHTERS

*To the Editor:*—The special report "Pursuing the Killers," in THE JOURNAL, Jan. 12, page 114, in describing the intense professional as well as lay organized activity to combat chemical poisoning—much of it accidental and in children—mentioned "the American Association of Pediatrics" as "a pioneer poison fighter." This typographical slip gives me an opportunity to identify the organization by its correct name, the American Academy of Pediatrics, and to add a brief comment to show that the American Academy of Pediatrics could more properly be credited as "the" pioneer poison fighter. The academy is responsible for initiating and continuing to furnish the necessary motive power through ideas and organization not only to make possible the wide range of professional and lay organized activity described in the article but to keep the movement in high gear.

The academy in 1950 created a committee on accident prevention. One of the first acts of the committee was a fact-finding survey of accidents seen in pediatric practice. This study revealed that accidental poisoning was very common. It was found that physicians wanted help, especially information on the toxic properties of common household agents and the treatment of poisoning. The committee conceived the idea of establishing poison information centers in community hospitals and developing a manual which would furnish information to the practicing physician. As a member of the committee, Dr. Edward Press, who was then in Chicago, was asked to take responsibility to develop this project. Through his initiative and imagination, the Illinois chapter of the American Academy of Pediatrics sponsored the first poison control center. This demonstration was made possible by the assistance of the Chicago Board of Health, the cooperating hospitals, the staff of the American Medican Association's Committee on Pesticides, and other Illinois groups.

The Academy of Pediatrics accident prevention committee was also responsible for the statement which first called attention to the frequency of aspirin poisoning in children and suggested measures to reduce this hazard. This later became a joint statement of the American Medical Association Committee on Toxicology and the American Academy of Pediatrics, and was adopted voluntarily by representatives of the pharmaceutical industry at a meeting sponsored by the Food and Drug Administration.

In 1955 the accident prevention committee of the academy prepared the first reference guide to the chemical constituents of common household substances together with treatment recommendations for children. This was written by Dr. Press and was field-tested in the poison control centers which soon sprang up after the Chicago demonstration. The first edition of the manual "Accidental Poisoning in Childhood" was printed through a grant to the Academy of Pediatrics from Johnson & Johnson of New Brunswick, N. J. Copies of the publication are available through the American Academy of Pediatrics, 1801 Hinman Ave., Evanston, Ill.

The article in THE JOURNAL referred to the prospect of establishing a clearing house for the exchange of vital information from various poison control centers. I am happy to report that, through the efforts of the American Academy of Pediatrics, the American Public Health Association, and the American Medical Association, the Department of Health, Education, and Welfare has recently announced the establishment of a national clearing house in the accident prevention unit of the United States Public Health Service.

In closing, I should point out that the tremendous work done on this poisoning problem in all parts of the country and the creation of, at the present time, 44 poison control centers is not a spontaneous development but can be traced to a large degree to the state committee organization of the Academy of Pediatrics. The state chairmen of the Academy of Pediatrics in virtually every state have set up state accident prevention committees. Since the purpose of Medicine at Work is to call attention to the public spirit of American physicians, I would like to point out that these enthusiastic and dedicated pediatricians on state committees exemplify the highest ideals of American medicine. Their work has been done largely through their state and county medical society memberships and their participation in the affairs of service clubs, the Parent-Teacher Association, and other child health and safety groups. Thus the concern of these physicians to reduce accidents in children has become "a program"—and properly so—of these local groups. When we consider what has been accomplished in preventing deaths from accidental poisoning in children in the past seven years as well as in reducing other accidents in children, we must give a full measure of credit to the efforts of all these physicians who work unsung at the community level.

GEORGE M. WHEATLEY, M.D.
District Chairman
American Academy of Pediatrics
1 Madison Ave.
New York 10.

## GASTROINTESTINAL HEMORRHAGE AND DRUGS

*To the Editor:*—Dr. Irving Brick in his paper "Early Diagnosis in Massive Upper Gastrointestinal Hemorrhage," which appeared in THE JOURNAL, April 6, page 1217, has commented on the importance of salicylates as a cause of gastrointestinal bleeding, particularly in patients with peptic ulcer.

The significance of this relationship is emphasized by two recent publications on the subject. Brown and Mitchell (*Gastroenterology* 31:198-203 [Aug.] 1956) stated that hemorrhage followed the ingestion of salicyl compounds in 69.5% of their series of patients with bleeding duodenal ulcer. Interestingly enough, 77%

(seven) of their patients with perforated peptic ulcer had a history of salicyl intake. Kelly (*Am. J. M. Sc.* 232:119-128 [Aug.] 1956) reported that 20% of a series of patients with bleeding peptic ulcer were receiving salicylates when symptoms developed. He also pointed out that the records of 32% of 49 patients with unexplained upper gastrointestinal bleeding revealed a history of salicylate therapy in progress for various conditions when the bleeding occurred.

Findings such as mentioned above should alert the practitioner to the fact that salicylates must at all times be prescribed with caution and must be avoided in patients with gastrointestinal distress.

George X. Trimble, M.D.
Director of Medical Education
Medical Director
St. Elizabeth Hospital
Youngstown 4, Ohio.

## EXPLOSIONS IN OPERATING ROOMS

*To the Editor:*—In the summary in The Journal (Foreign Letters, Nov. 3, 1956, page 1001) of the report of a working party on anesthetic explosives, there are errors in the passage about operating theater floors which give the impression that such floors should be nonconducting. It is suggested that the words "without such floors" should read "with such floors," "a new, nonconductive floor" should read "a new, conductive floor," and "nonconducting paint" should read "conducting paint." The whole passage would then read:

"Only 5-10% of operating rooms in Great Britain have nonconducting floors (rubber or cork). In operating rooms with such floors the danger of explosion can be decreased by dampening the floor or by putting a damp sheet down if evaporation is rapid. If explosive anesthetics are used routinely, the only safe procedure is to lay a new, conductive floor. The use of conducting paints for floors is being investigated."

This summarizes accurately the findings of the working party on the subject.

P. M. Williamson
Secretary of the Working Party
Ministry of Health
Savile Row
London, W. 1, England.

## RADIOACTIVE FALL-OUT OVER CITY

*To the Editor:*—In The Journal, March 9, page 803, Heise and Heise have suggested that a city may well offer an added measure of safety from radioactive fall-out. I disagree with their meteorological interpretations and would like to explain my objections.

They argue that the rising currents over a warm city account for the lower spore and mold concentration on the leeward side of the city. However, since a city is not a source of spores and molds, it is difficult to distinguish between their explanation and a simple decrease in concentration farther from the source. Besides, the fall velocity of radioactive particles in the first few hundred miles from a nuclear explosion is from 10 to 1,000 times greater than that of spores, molds, or pollen. The slight upward current over a city which might support spores, etc., will have no important influence on such rapidly falling radioactive particles. Heise and Heise's experiment in which a heated area in a small box simulated a warm city is unrealistic. The horizontal wind in nature will disturb the simple convective cell of the experiment. Further, as just noted, the lycopodium spores used by them fall at negligible rates compared with real radioactive particles of close-in fall-out.

I can report an experiment relevant to fall-out over cities. At many places over the United States, the Weather Bureau operated fall-out collectors at ground levels for the Atomic Energy Commission both within cities and at nearby airports. We find no systematic difference which would suggest an ameliorating influence of the city.

There is no doubt that a city disturbs air flowing over it, but the upward currents which might ward off radioactive danger are too weak to influence the descent of large fall-out particles. No significant meteorological benefit is believed to accrue from the city's warmth. On the other hand, the city may still be safer during and after fall-out than the nearby countryside because of the availability of shielding and decontamination facilities, as well as avoiding problems of evacuation.

Lester Machta, Chief
Special Projects Section
Office of Meteorological Research
U. S. Weather Bureau
Washington 25, D. C.

## POSTPARTUM ELECTROSHOCK THERAPY

*To the Editor:*—The article on electroshock therapy during the puerperium, by Impastato and Gabriel, as published in The Journal, March 23, page 1017, prompted this submission. In July, 1947, because of necessity, I gave electric shock therapy to a 23-year-old patient on the eighth day after cesarean section. It was necessary to use 1 Gm. of amobarbital sodium intravenously every eight hours after delivery to alleviate the symptoms of excitement and hyperactivity. Finally, on the eighth day after surgery, with the use of curare intravenously, electric shock therapy was started and given daily for eight days, with a good result in the alleviation of symptoms.

A review of my records indicates that I have had to use electric shock therapy as an emergency measure for the control of symptoms in eight patients during the period of gestation. I have given electric shock therapy to one patient during the eighth month of pregnancy, to two patients during the seventh month, to three patients during the sixth month, and to five more patients who were less than six months pregnant.

I was the first practicing psychiatrist in Arkansas to use electric shock therapy on private patients, and decisions had to be made because of emergency measures. My records for the past 10 years include the treatment of 12 patients with postpartum psychoses who received shock therapy between the 5th and 15th days after delivery of the child.

Louis A. Cohen, M.D.
24 Pine Manor Dr.
Little Rock, Ark.

# MISCELLANY

## REPORT TO THE CHAMBER OF COMMERCE OF THE UNITED STATES AND THE NATIONAL ASSOCIATION OF MANUFACTURERS

William L. McGrath

In January, 1956, the directors of the Chamber of Commerce of the United States adopted a resolution on continued Chamber participation in the International Labor Organization. The board of directors of the National Association of Manufacturers did likewise in February, 1956. Both resolutions made clear that future participation in the ILO was contingent upon future developments. For example, the NAM resolution reads, "If no change for the better in the activities and structure of the ILO is effected in the course of the 1956 sessions, the NAM will withhold its participation in the nomination of members for the 1957 delegation."

Has any "change for the better" been effected during the 1956 ILO sessions? This report is submitted in answer to that question.

### Major Issue

The major issue before the ILO in 1956 is increased communist participation. The issue is in fact broader than communism, as it embraces socialism and nationalization of industry as well. It so overshadows other considerations that this report will be limited to that subject.

You may recall that at the March, 1955, meeting of the ILO governing body, instead of approving (as had been proposed) an amendment to the ILO constitution which if adopted might disqualify communist so-called employer and worker delegations, the governing body authorized the appointment of a committee (McNair committee) to study and report on the extent of freedom of employers and workers' organizations from domination and control by their governments. No further action on the communist issue was taken, pending completion of the McNair report. At the June, 1955, conference "tripartite delegations" from eight communist countries attended and participated. This brings us up to 1956.

### March, 1956, Meeting of the ILO Governing Body

The McNair report was completed in February, 1956. At its March, 1956, meeting the governing body decided that, although there might be an exchange of views on the report at the June, 1956, conference, it would not be officially considered until the November, 1956, governing body meeting.

### June, 1956, Conference

At the June, 1956, conference a challenge to the credentials of communist so-called employers was for the second time rejected by the conference (the first time was in 1954) and tripartite delegations from nine communist countries attended and participated (Roumania had meanwhile been admitted).

In his report on this conference, Charles H. Smith Jr., who served as the U. S. employer delegate, stated: "In all honesty, I cannot report any major improvement in the ILO itself as evidenced at the 1956 Conference." In a letter to Mr. Mitchell, Secretary of Labor, dated Oct. 10, 1956, Mr. Smith said: "It is my belief that the United States cannot afford to continue to participate in ILO activities unless we take immediate concerted action to counter the socialistic and communistic propaganda that is so widely distributed at any ILO meeting."

As you can see from the following, the likelihood of any such concerted action is remote indeed.

### Meetings in Washington

On Oct. 17 I wrote Mr. Wilkins, Assistant Secretary of Labor, suggesting that, in view of the importance of the forthcoming discussion of the McNair report at the November governing body meeting, it might be desirable to hold a conference on the subject.

On Oct. 22 I attended such a meeting, at which were present representatives of the Labor, State, and Commerce Departments. They asked me what I intended to do at the governing body meeting. I told them that above all else I intended to press for an amendment to the ILO constitution, which, if adopted, would exclude communist so-called employers from participation in the ILO. I asked them what government intended to do, and they said they did not know.

A second meeting was held in Washington on Nov. 7. Mr. Wilkins was present at this meeting, and also Mr. Delaney, U. S. worker representative on the governing body. I restated my position, but urged that government should take the lead in standing on the principle that the integrity of the ILO has been violated and that the constitution should be amended. I was told that the government "felt reluctant" to take such a position, but that as a matter of fact it as yet had no position on the McNair report.

### November, 1956, Governing Body Meeting

At this meeting discussion of the McNair report overshadowed all other issues. The substance of the report (although almost 2,000 pages long) can be summed up as follows: Although in some countries employers are in fact government men, and unions merely instruments of government, nevertheless in the interest of universality this situation may as well be accepted.

The main importance of the report is that it discloses the growing extent of nationalization of industry in practically every part of the world except the United States.

Early in the debate on the report the free employers took definitive action. On the basis of facts disclosed in the report they introduced the following resolution, which was in substance identical with a resolution which originally had been proposed by the workers' group at the November, 1954, meeting of the governing body: "The Governing Body decides to place on the agenda of the 1957 Session of the International

United States Employer Representative to the International Labor Organization Governing Body.

Labor Conference the amendment of Article 3, paragraph 5, of the Constitution so as to ensure that worker and employer representatives can only be appointed after nomination by organizations of workers and employers which are free and independent of their governments."

Such an amendment would disqualify communist so-called employer delegations. I spoke in support of this resolution. Copy of my address is attached hereto (see page 327), and I refer you to that text for a full explanation of the basic issue involved.

All 10 employer members stood solidly in favor of the resolution and spoke eloquently on its behalf. But we were assailed by a barrage of opposition oratory from the worker and government side, that revealed as never before the hopelessness of the free employer's position in the ILO.

The labor-government-socialist majority, now well in control, openly, triumphantly, and even jeeringly displayed their satisfaction in riding roughshod over the free employers and relegating free enterprise to a secondary position in the ILO.

We were told that nationalization of industry was on the march the world over, and we must therefore accept communist government agents as employers. This argument was advanced chiefly by socialist worker and government members of the governing body, which has only one communist member. In supporting the communist cause the socialists were protecting their own right to send government men from nationalized industries to the ILO as employer representatives.

As an example of the brotherhood between socialism and communism, it was actually proposed that there should be two classes of employers within the ILO—free employers representing private enterprise, and communist and socialist employers representing nationalized industries. This led to speculation as to whether there might be two classes of workers in the ILO—one representing free trade unions, and the other representing government-run unions serving in fact as agents of the state.

The only supporter of the free employers was the government of Free China! Here is the vote:

| | |
|---|---|
| *For* the resolution: | |
| All employer members of the governing body | 10 |
| The government of Free China | 1 |
| | 11 |
| *Against* the resolution | |
| All worker members of the governing body | 10 |
| All government members except Free China | 19 |
| | 29 |

The governing body consists of 20 governments, 10 employers, and 10 workers.

Mr. Delaney, the U. S. worker member, said he was in favor of the resolution but was voting against it because he knew it would have no chance of passing. The U. S. government spoke and voted against the resolution.

After the defeat of the resolution it was proposed by Mr. Delaney that the ILO should set up machinery in the office to investigate further the extent of freedom of association in member countries. The proposal was broadened to include investigation of "methods of working" of the conference, including committees, and was then approved by the governing body.

All that happened was that upon one investigation, that had lasted a year and a half, there was superimposed another investigation that will drag into years. Absolutely nothing was done to resolve the issue involved.

## Conclusions

The above action dramatized the fact that the tripartite structure of the ILO has long since become a myth. Besides government in the government group, we now have government in the employers' group and government in the workers' group. The ILO is now to all intents and purposes an international government organization run mainly along political lines under the domination of advocates of collectivism, with free employers possessing no influence of any consequence and serving chiefly as whipping boys for the communists and the socialists.

When the views of the free employers of the world no longer carry any appreciable weight in the ILO—when the socialist-communist government and labor majority in the ILO announce that free employers must "coexist" with communist agents in ILO employer committees—when governments invade both the employer and worker groups, and make a mockery of tripartite representation—when further nationalization of industry is openly announced as a desired goal—why should the NAM and the U. S. Chamber continue to participate in the ILO?

I believe we can accomplish far more outside the organization than we can within it. As long as we stay in the ILO, we must carry its label. Do we not participate in its meetings and its findings? How can we condemn something of which we are a part? But if we withdrew from the ILO, we could label it for what it is. We could explain to the world that we are opposed to the majority philosophy of the ILO, that we do not believe in it, that we stand for free competitive enterprise instead of socialism and communism.

Our dramatic action would arouse sufficient interest so that we could tell the story of what has happened to the ILO, and it would be listened to, both at home and abroad. We could announce that we proposed to have nothing further to do with a communist-socialist dominated organization devoted to the cause of nationalization of industry.

We would be helping the free employers of other countries. They are too afraid of their governments, or too committed to personal careers within the ILO to get out of it. But we are free. We can take an action that they will envy—and perhaps our courage may help them to do likewise.

And finally, withdrawal by the NAM and the U. S. Chamber, on the ground that we will not sit with communist agents as employers, will support the action taken by the Senate of the United States on April 19, 1956, when it passed a resolution denying any increase in ILO appropriations as long as communist delegates allegedly representing employers and workers are allowed to vote in the ILO.

The U. S. government will no doubt press us, as they have before, to stay in the ILO. I am not impressed by government arguments. Our government has assured me that they fully understand the extremely serious nature of the situation within the ILO, but they do absolutely nothing about it. At the governing body meeting, not one single government came forward with a suggestion for a possible solution to the present dilemma. Nothing is going to be done unless somebody takes action.

Suppose the U. S. Chamber and the NAM should withdraw, and the government would then appoint an employer delegation from some other source. Would that affect us adversely? I think not. Our position would be simply that if someone else wants to sit with the communists, it is all right with us—but we do not want to.

## Recommendation

In view of all of the above, I recommend that, in accordance with resolutions previously passed, and in the light of the fact that there has certainly been no change for the better in the activities and structure of the ILO, the NAM and the U. S. Chamber no longer participate in the nomination of employer delegations to the ILO.

**Statement by W. L. McGrath, United States Employer Delegate in ILO Governing Body, November 20, 1956.**

I wish to support most emphatically the conclusive arguments presented by Mr. Waline on behalf of the proposed amendment to the constitution of the ILO.* I regard this amendment as essential to reaffirm a principle which has been inherent in the ILO constitution from the very beginning.

The constitution states, in paragraph 1 of Article 3, that, of the four delegates from each country, "two shall be government delegates and the two others shall be delegates representing respectively the employers and the work-people of each of the members." The constitution then goes on to say in paragraph 5 of Article 3: "The members undertake to nominate *non-Government* delegates and advisers chosen in agreement with the industrial organizations, if such organizations exist, which are most representative of employers or work-people, as the case may be, in their respective countries."

The vital word in that paragraph is "non-Government." This paragraph assumes that employer and worker delegates must be nongovernment. Taken in conjunction with paragraph 1 of Article 3, there can be no possible doubt that such was the intent of the framers of the ILO constitution.

But it was not pinned down in sufficiently definitive language. How could the framers of the ILO constitution possibly have foreseen the sorry spectacle of such complete government domination over the affairs of men that in some nations free organizations of employers and workers would be nonexistent and the only voice allowed to speak would be the tyrannical voice of government?

And so, in the June, 1954, conference, when the credentials of communist so-called employer and worker delegations were challenged, the constitution was found wanting. The majority of the credentials committee claimed, and the majority of the conference agreed, that there were no words in the ILO constitution that specifically stated that freedom of domination and control by governments must be a condition of employer and worker representation in the ILO.

Gentlemen, that is exactly the point. This is a deficiency in the wording of the constitution. It is now proposed to correct that deficiency by inserting a paragraph which will specifically spell out what the framers of the constitution intended, and what the constitution as a whole has implied from the very beginning.

Let me give you an analogy from the history of the United States. The Constitution of the U. S. A., as originally ratified, implied certain rights and freedoms. But some of our statesmen said—this is not enough. We cannot depend upon implication and interpretation alone. We must get these things down in black and white, so no one can get around them. And so, as you know, we enacted 10 amendments to our Constitution, which together are known as our Bill of Rights. All these amendments did was to spell out specifically what everyone knew had been the intent of the Constitution from the beginning. But the effect was an effectual safeguarding of rights and liberties for all time.

For example, the United States Constitution as originally drafted implied freedom of religion and of the press. But was mere implication sufficient protection? We decided it was not. Therefore, we added an amendment that states "Congress shall make no law respecting an establishment of religion or prohibiting the free exercise thereof, or abridging the freedom of speech, or of the press." Gentlemen, that was not a change. It was simply an affirmation of original principles. And that is exactly what is proposed in this case.

The net effect of the proposed amendment to the ILO constitution is simply that of affirming the principle, stated in paragraph 5 of Article 3, that employer and worker delegates shall be nongovernment.

Let us stick to this basic point, and not get involved with specious philosophical arguments having to do with "universality"—a term which, incidentally, I have yet to find in the ILO constitution.

What has brought this issue to a head is the brazen endeavor of the communist countries to foist government men upon us as representatives of employers and workers.

Is there any doubt as to the facts with respect to this situation? Let me quote just two brief sentences from the opinion of Mr. Justice Cornelius, included in the McNair report. As to unions in communist countries, he states: "It appears clearly that, under this system, the trade unions constitute an agency of the government." As to directors of industrial undertakings in communist countries, Mr. Justice Cornelius states: "It seems impossible to deny that their relationship with the government is one of direct subordination, leaving no scope for freedom of action on their part."

The communists have put forward the claim that the functions of managers in industrial undertakings in communist countries are practically identical with the functions of free employers. Well, I recently received a copy of the June, 1956, issue of *Industry and Labor*, published by the ILO, which contains a summary of the "Reorganization of State Industry in Czechoslovakia." I quote in part from this report: "The work of each state undertaking is directed by the competent minister in accordance with principles laid down by the government. Each minister is required to allocate the tasks outlined in the state plan to the various undertakings, administer and supervise their implementation of the plan, direct the undertakings' wage and capital investment policies, and supervise the selection and allocation of supervisory and managerial staff." The report then goes on to say that each undertaking has a manager. Well, what does he manage? I would say that he must manage to do what government tells him to do, or else.

Have we not had enough of this farce? After what has happened in Hungary, can anybody sustain the claim that there are free associations of workers or employers in communist dominated countries, or that their so-called employer and worker delegations to the ILO can possibly represent anything but government and the Communist Party?

Gentlemen, let us secure the enactment of the proposed amendment, which will reaffirm the long-established structure of this organization. By doing so, we are merely confirming the original intent of the framers of the ILO constitution.

If, on the other hand, we fail to enact this amendment, we will have allowed the ILO constitution to lapse by default. We will have given our consent to a violation of its principles

*The text is as follows: "The Governing Body decides to place on the agenda of the 1957 Session of the International Labor Conference the amendment of Article 3, paragraph 5, of the Constitution so as to ensure that worker and employer representatives can only be appointed after nomination by organizations of workers and employers which are free and independent of their governments."

and sacrificed our integrity upon the altar of political expediency. We will stand before the world as a prime example of international hypocrisy, and earn the public disrespect which can only be the forerunner of disintegration.

# LAW DEPARTMENT

## MEDICOLEGAL ABSTRACTS

**Prenatal Injuries: Liability for Injuries to Embryo of Fetus.**—This was an action by a child for alleged tortious injuries sustained by her while she was an embryo or fetus in her mother's womb. From a judgment for the plaintiff, reversed by the court of appeals, the plaintiff appealed to the Supreme Court of Georgia.

The plaintiff contended that she received prenatal injuries when the automobile in which her mother, who at the time was about six weeks pregnant with the plaintiff, was riding was struck by an automobile negligently operated by the defendant. The defendant demurred to the complaint on the ground that the plaintiff was not quick in her mother's womb at the time of the accident.

The Supreme Court of Georgia pointed out that the statutes of that state give every person tortiously injured a right of action. In fact it quoted one of its prior decisions to the effect that, where a child is born after a tortious injury sustained at any period after conception, he has a cause of action. While we realize, continued the court, that cases such as this might present extreme difficulties as to proof, we are not concerned with that question here. The petition alleges that the plaintiff who is now in life received prenatal injuries, caused by the alleged negligent operation of an automobile in which the plaintiff's mother was riding while pregnant, which resulted in the plaintiff's being born with a deformed right foot, right ankle, and right leg, and in passing upon the demurrer these allegations must be taken as true. If a child born after an injury sustained at any period of its prenatal life can prove the effect on it of a tort, it would have a right to recover.

Accordingly, the Supreme Court reversed the judgment of the appelate court and found in favor of the plaintiff. *Hornbuckle v. Plantation Pipe Line Company, 93 S. E. (2) 727 (Ga., 1956).*

**Workmen's Compensation: Compensability of Anxiety Neurosis.**—This was an action for a compensation award based upon an anxiety neurosis alleged to have arisen out of an industrial injury. From an adverse decision the defendant appealed to the Supreme Court of Florida.

In June, 1953, the claimant was injured in the course of his employment in the defendant's mill. The injury, to his right leg, aggravated a condition of varicose veins that he had suffered in both legs for some years. A thrombophlebitis that developed in his right leg and extended to his lung (a pulmonary embolus) was successfully treated. A year later he was again treated for thrombophlebitis in the right leg, and a ligation of the saphenous vein was performed to prevent another pulmonary embolus. In July, 1955, the compensation board found that the claimant was depressed, apathetic, and in constant fear that, if he resumed his usual employment as a millworker, the long periods of standing would cause thrombophlebitis in his left leg and another pulmonary embolus therefrom. It, therefore, held that the claimant's anxiety neurosis was, under these circumstances, a compensable injury. On appeal, the defendant contended that the claimant's neurosis was too remote from the injury to sustain an award.

The Supreme Court of Florida said that the sole issue was whether or not the claimant was entitled to compensation for a disability caused by an anxiety neurosis. When there has been a physical injury, the full disability, including the effects of the neurosis, is compensable. It must appear, however, that the neurosis was the direct and immediate result of the industrial injury. The casual connection of the neurosis with the accident must not be remote. Here, said the court, the claimant's neurosis did not result directly and immediately from his injury. The Commission had reasoned (*a*) that the injury was to claimant's right leg, (*b*) that the thrombophlebitis developed by aggravation of a preexisting disease, (*c*) that the thrombophlebitis resulted in a disease known as pulmonary embolus, (*d*) that this pulmonary embolus resulted in a disease known as an anxiety neurosis. The Supreme Court said that the industrial injury could not possibly result in the thing feared (a pulmonary embolus) because the saphenous ligation admittedly will prevent a pulmonary embolus from developing as a result of a blood clot in his right leg. While a court in doubtful cases resolves many doubts in favor of a claimant under the Workmen's Compensation Act, where the claimant's neurotic disability is only remotely related to the industrial injury, industry should not be required to bear the cost of the disability. Therefore, the ruling in favor of the claimant was reversed. *Superior Mill Work v. Gabel, 89 So. 2d 794 (Fla., 1956).*

**Malpractice: Hospital's Liability for Nonprofessional Acts of Its Servants.**—This was an action for damages for burns alleged to have been caused by the negligence of the defendant surgeon and the defendant hospital. From a judgment in favor of the surgeon but against the hospital, the hospital appealed to the Supreme Court of Iowa.

The plaintiff entered the defendant hospital for an operation on her back, which was to be performed by the defendant surgeon. When she was taken to the operating room, she was placed face down on the operating table and "preped" and draped for surgery. While the "preping" was going on, the surgeon retired to the scrub room to scrub for the operation. "Preping" refers to the preparation of the skin in the surgical area, including shaving, cleansing, and things of that nature. The surgeon had the right to determine how plaintiff would be "preped," but he had given no special instructions in this instance and did not know what solutions were used in the final preparation. When the surgeon returned to the operating room, he observed nothing objectionable about the "preping" and proceeded with the operation, which took four hours. After the operation, a dressing was applied to the sur-

gical area, and the plaintiff was returned to her room. The defendant surgeon did not see her again until the next morning. When the surgeon saw the plaintiff the next morning, he expressed surprise as he observed the severe burns on her abdomen. He said there had been no explosion during the course of the operation or in his presence, but he gave no explanation as to the cause of the burns. The plaintiff tried to find out what happened, but nobody ever told her and no evidence was introduced at the trial to enlighten the court as to what happened. According to the nurses' records, doctors expressed the opinion that the blisters were "apparently from ether."

The crux of the case, said the Supreme Court of Iowa, resolves itself around two main issues upon which this court has not previously made pronouncement and upon which there is little authority elsewhere. The first issue, stated simply, is whether or not in cases of this nature it is necessary under the doctrine of *res ipsa loquitur* for plaintiff to prove what instrumentality or instrumentalities caused her injury; and the second is what liability a corporate hospital has for the acts or omissions of its officers, employees, or attachés when a patient under anesthesia is injured by lack of due care while in the hospital for treatment or surgery.

The doctrine of *res ipsa loquitur*, said the court, is a simple understandable rule of circumstantial evidence with a sound background of common sense and human experience, and difficulty comes only when we attempt to transform it into a rigid formula, which arbitrarily precludes its application in many cases where it is most important that it be applied. It is regarded as a presumption, throwing upon the party or parties charged with the duty of producing evidence of the circumstances, to come forth with the evidence, whether culpable or innocent, which is particularly accessible to him or them but inaccessible to the injured person. In the instant case the plaintiff placed herself in the care and custody of the defendant surgeon and the hospital employees, and, from the time she lost consciousness until she awakened some nine and one-half hours later, she did not know what instrumentalities were used on her nor how she was injured. The injury was of a kind that ordinarily does not occur in the absence of someone's negligence. Whether the doctor or the hospital employees were then acting in a professional, semiprofessional, or nonprofessional capacity, she would not know. She brought action against the surgeon in charge and properly assumed that, if the injury occurred during the operation proper, by him or his temporary assistants in a professional capacity, he would be liable, but, if the injury occurred while defendant hospital was undertaking to perform other nonprofessional or simple manual acts of an administrative nature through its servants, then, of course, the hospital would be liable. It was sufficient that plaintiff disclosed that the injury resulted from an external force applied while she lay unconscious in the hospital, and we conclude that that satisfies the requirement that the plaintiff identify the instrumentality causing her injury. It is as clear an identification as such a plaintiff of her own knowledge may ever be able to make, and, under the doctrine of *res ipsa loquitur*, the law should require no more. We think, said the court, it is a just and logical conclusion that one who, while undergoing a surgical operation, sustains an unusual injury to a healthy part of her body not within the area of the operation, be not precluded from invoking the doctrine of *res ipsa loquitur* in an action against the doctors and nurses participating in the operation. The same thing must be said of the corporate hospital regarding its preceding or subsequent care of the patient. This is not altered by the fact that all the parties do not stand in such relation to one another that the acts of one may be regarded as the acts of the other and the injury may have been caused by the separate acts of any one of them, or by the fact that there were several instrumentalities and no showing as to which caused the injury or as to the particular defendant in control of it.

The defendant hospital also contended that the "preping" services rendered by the surgeon, nurses, and house physician were professional services, that the defendant hospital could not practice medicine or osteopathy, and that, therefore, it could not be responsible for injuries caused by such professional acts. The evidence showed that the "preping" had been done while the defendant surgeon was out of the operating room getting scrubbed up for the operation. We are aware, said the court, that there are cases that hold that "preping" is considered a part of the operation proper, and in some cases this may well be, especially where special "preping" is required. A careful study of the record in this case, however, fails to reveal that the "preping" done in this case was any more than the "standard" procedure or simple manual act done by servants or students of the hospital, and, therefore, we do not feel called upon here to decide whether "preping" generally is in fact the practice of osteopathy and surgery. The failure of hospital servants to do any such administrative or simple manual acts with due care would, of course, constitute negligence for which the principal may be held liable under the doctrine of *respondeat superior*, regardless of the servant's title, license, or professional position. In the absence of proof that any tasks being performed, with the exception of those of the surgeon, were of a professional nature, they must be found to be administrative. Clearly then, continued the Supreme Court, except when employees, regardless of class, were "loaned" or were engaged in the practice of osteopathy, this defendant hospital determined and directed their duties and made assignments. With those exceptions, it had "complete" control over the doctors and nurses employed by it. In such cases it seems only just and proper to require satisfactory proof by the master that its servant was not acting as its servant at the time or times in question. Although it is true, the court concluded, that the professional discretion of hosptal staff doctors cannot be controlled by the nonlicensed corporation, nevertheless even those individuals, while performing nonprofessional functions under the master-servant relationship, will not protect the corporation from liability for its servant's negligence.

Other contentions of the defendant hospital were also overruled, and the judgment of the trial court against the hospital was affirmed. *Frost v. Des Moines Still College of Osteopathy and Surgery, et al., 79 N. W. (2d) 306 (Iowa, 1956).*

# MEDICAL LITERATURE ABSTRACTS

## INTERNAL MEDICINE

**Erosive Gastritis in Cirrhosis: Influence of Portal Hypertension on the Gastric Mucosa.** E. D. Palmer. Am. J. Digest. Dis. **2**:31-36 (Jan.) 1957 [New York].

The importance of acute erosive gastritis lies in the suddenness with which it may lead to exsanguination. Among 38 cirrhotic patients with esophageal varices who died while under treatment by the author in the past 6 years as a direct result of hemorrhage, the hemorrhage was found to be originating from erosive gastritis in 4, from gastric or esophageal varices in 30, and from ulcer in the other 4 patients. It has been assumed that the mechanical venous back pressure of portal hypertension rather than a circulating metabolite is at fault when erosive gastritis develops in patients with cirrhosis. The reasons for this assumption are that there appears to be no correlation between the development of erosive gastritis and the degree of liver insufficiency and that erosive gastritis becomes rare after portal decompression. The purpose of the present study was to investigate the histopathology of the gastric mucosa in patients with portal hypertension due to cirrhosis in an effort to determine whether mechanical capillary damage in the mucosa, secondary to venous hypertension, is a proper explanation for the erosive process. Histological examination of the canine gastric mucosa after sudden production of portal hypertension by portal vein ligation shows that the increased venous pressure under these artificial conditions is reflected back into the vessels of the mucosa. When portal hypertension develops naturally and gradually in cirrhosis of the liver, however, the hypertension is contained within the submucosa and no vascular dilatation develops within the mucosa.

Degenerative gastritis with a prominent erosive element, leading to blood loss, is an important complication of cirrhosis with portal hypertension. Both gastroscopically and histopathologically the gastritis appears entirely similar to that encountered in patients who have no liver or portal disease. The most significant abnormality is necrobiosis of the mucosal neck stratum. The blame cannot be placed on interstitial hemorrhage from the mucosal capillaries, nor can mucosal plethora with capillary stasis be considered an etiological factor. The presence of venous dilatation in the submucosa suggests the possibility that secondary mucosal hypoxia, due to stasis without mucosal engorgement, might be sufficient, since it is known that the neck stratum is particularly susceptible to the hypoxic influence of ischemia. Although this has by no means been proved, it seems a more acceptable explanation than the only reasonable alternative, that of the influence of a noxious circulating metabolite.

**A Contribution to the Clinical Study of Pigmentary Cirrhosis: Report on 31 Cases.** M. Girard, M. Plauchu, J. Fayolle and R. Bastide. J. méd. Lyon **38**:39-71 (Jan. 20) 1957 (In French) [Lyon, France].

The authors report on 31 patients with pigmentary cirrhosis. Pains in the right hypochondrium or in the epigastrium were present in most patients. Dyspepsia, circulatory disturbances, gastrointestinal hemorrhage, and icteric episodes were neither frequent nor marked. Splenomegaly, collateral circulation, and ascites were rare. Melanoderma, which is a classic symptom of the disease, was not uniform in its cutaneous distribution or in its color intensity. This symptom is latent in most patients and is often overlooked. Diabetes that was mild but difficult to control and insulin instability were observed in 12 patients. The curve of provoked hyperglycemia showed that some patients did not tolerate glucose. More than half of the patients showed no signs of sexual impairment. Major disturbances of the sexual organ were rare; other endocrine disturbances were rare.

Acute heart failure occurred in 2 patients under 50 years of age. Latent or mild forms of cardiac insufficiency frequently associated with pigmentary cirrhosis were observed in patients in the "vascular" age, only. The diagnosis was based on the presence of hypertrophic cirrhosis and cutaneous pigmentation. Biological and anatomic tests were given because of the monosymptomatic manifestation of the disease in most patients and because the pigmentation was latent in many cases. Biological tests were considered positive only when the iron content of the serum was above 260 mcg. Hormonal tests did not prove reliable. Laparoscopy was the most frequently used test. Needle biopsy was used when all other tests had given equivocal results.

**Hepatitis as Occupational Disease Among Physicians.** C. Frieberger, M. Haider, E. Rissel and F. Wewalka. Wien. klin. Wchnschr. **69**:44-47 (Jan. 18) 1957 (In German) [Vienna].

A questionnaire was sent to physicians and lawyers in Vienna, Lower Austria, and Burgenland in an attempt to ascertain the incidence of hepatitis in physicians (using the lawyers as controls) and to eval-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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uate it with regard to the problem of occupational risks. They were asked whether and when they had had jaundice that was not the sequela of gall bladder disease. They were also asked about the time of the occurrence of the illness and its duration and whether it occurred simultaneously with active military service during the war. Of the physicians, 29.7% had hepatitis after the age of 18 years, as compared to 22.9% of the lawyers. An incidence of 16.8% was found among the physicians as compared to 8% among the lawyers, when cases occurring in the course of active military service during the war were excluded. An incidence of 23.8% was found among medical specialists who still were working in hospitals when they received the questionnaire, as compared to 15.7% among general practitioners working in their offices and in hospitals.

These data suggest that physicians are exposed to an increased occupational risk with regard to hepatitis and that this risk is even greater with hospital work. It is emphasized that hepatitis is a reportable occupational disease in Austria and that the incidence of hepatitis exceeds that of other infectious diseases in the course of practicing medicine. Prophylaxis of hepatitis has not received enough attention because of the long incubation period of homologous serum jaundice. Comprehensive enlightenment of the physicians and the nursing personnel concerning the various possible ways of transmission of the viruses causing hepatitis and concerning the associated occupational risk is indispensable.

**Acute Recurrent Rhabdomyolysis (Paroxysmal Myohæmoglobinuria): A Report of Three Cases and a Review of the Literature.** D. H. Bowden, S. H. Jackson and N. F. Walker. Medicine **35**:335-351 (Dec.) 1956 [Baltimore].

Although paroxysmal myohemoglobinuria was first described in 1910, only 25 cases have been reported since then, and the authors present observations on 3 additional cases. The important data on all 28 patients are summarized. The disease occurs in paroxysms that are heralded by muscle pains and weakness, followed shortly by the passing of dark red-brown urine. The provisional diagnosis is made by demonstrating a hemoglobin-like pigment in the urine in the absence of hemoglobinemia, but absolute proof of the diagnosis depends on the spectroscopic identification of myohemoglobin in the urine. Since the spectroscopic absorption bands of myohemoglobin are similar to those of corpuscular hemoglobin, the differentiation of the 2 pigments formerly required the use of expensive equipment. Now a method has been developed that does not require such equipment. Studies carried out by the authors indicate that the symptom complex of paroxysmal myohemoglobinuria is the result of a pathological process in striated muscle, and, in conformity with this concept, they propose that the condition be renamed "acute recurrent rhabdomyolysis." Myohemoglobin is but one of many substances that are released from the muscles into the blood and excreted by the kidney. There is no reason to suspect that there is any abnormality in the structure of the myohemoglobin liberated or that this substance is in any way implicated in initiating the attacks. The term myohemoglobinuria describes a single feature only and in no way indicates the underlying pathological process.

Since the authors observed 3 patients with this supposedly rare disease in the course of 2 years, they believe that it is perhaps more common than the number of reported cases indicates. The disease causes widespread muscle damage, but seems to involve only striated muscles. There are indications that 2 distinct forms of the disease exist. In 1, the attacks are always precipitated by exertion; in the nonexertional type, acute attacks may be associated with a variety of factors or may appear spontaneously. Genetic factors may operate, but the exact mode of inheritance has not been established. Acute recurrent rhabdomyolysis is a serious disease. Repeated attacks are to be expected, there may be residual atrophy of muscles, and the condition is sometimes fatal.

**Carbon Tetrachloride—An Underrated Hazard.** G. E. Joron, C. H. Hollenberg and E. H. Bensley. Canad. M. A. J. **76**:173-175 (Feb. 1) 1957 [Toronto].

Carbon tetrachloride can produce fatal liver damage, but in the last 15 years it has been shown that the most common lesion in poisoning with this solvent and dry cleaning agent is acute injury to the tubules of the kidney producing acute renal failure or lower nephron nephrosis. The terms acute renal failure or acute tubular injury are to be preferred to lower nephron nephrosis. Poisoning with carbon tetrachloride may follow its inhalation, ingestion, or absorption through the intact skin. Ingestion of alcohol before, during, or soon after exposure greatly increases the likelihood of renal damage. The histories of 12 patients with poisoning due to carbon tetrachloride are presented. In the first 8 of these, there was exposure to alcohol as well as to carbon tetrachloride; severe renal damage followed in every instance. In the remaining 4 patients, there was no ingestion of alcohol and no renal damage. None of the 12 patients had serious hepatic involvement.

A patient who has been exposed to carbon tetrachloride, particularly if there was concomitant alcohol ingestion, deserves close observation. Nausea and vomiting may occur without evidence of involvement of the liver or kidneys. Elevation of blood pressure level and back pain suggest renal involvement. The early laboratory investigation should include examination of the urine, which in a typical case of acute tubular injury is scanty, has a specific gravity of from 1.010 to 1.015 and contains albumin and many red and white blood cells and casts. Under these circumstances azotemia will be present. Liver function should be studied by measuring the serum bilirubin and cephalin flocculation or by a similar test.

These patients usually respond to conservative therapy and seldom need any form of dialysis. However, they should be in a hospital where electrolyte studies can be carried out. The principal danger is administration of excessive amounts of water and electrolytes during the phase of oliguria leading to death from pulmonary edema. There are hazards in

faulty diagnosis and treatment, but the greatest hazard is the lack of awareness of the dangers inherent in the use of carbon tetrachloride. The main problem is prevention of exposure. Carbon tetrachloride should not be sold without suitable warning labels, and the warnings should be strong enough to discourage its use in the household and small industries. In many large industries less toxic compounds now replace carbon tetrachloride as a solvent and dry cleaner.

**Patients with Hyperglycemia Treated with Thioctic Acid.** G. Schirosa and L. Pagliaro. Riforma med. **71**:32-35 (Jan. 12) 1957 (In Italian) [Naples].

The authors report on the treatment with thioctic acid of 29 patients with hyperglycemia. The drug was given 2 or 3 times a day always before meals; 2 patients received it orally, and the others received it either intramuscularly or intravenously. The patients were divided into 2 groups. The 1st group (13 patients) was treated with thioctic acid only in doses of from 50 to 70 mg. per day. The effect was evident on the 2nd day after starting this treatment. The 2nd group (16 patients) was treated with from 30 to 60 mg. of thioctic acid given daily in addition to insulin. The drug had a beneficial effect on the blood sugar level of all patients; those with mild hyperglycemia became normal. The combination of thioctic acid with insulin permitted reduction of the dose of insulin in patients with severe hyperglycemia. The best results were obtained in patients with marked hepatic deficiency. The thioctic acid increases the glycogen synthesis in the liver.

**Acute Respiratory Disease in University of Wisconsin Students.** A. S. Evans. New England J. Med. **256**:377-384 (Feb. 28) 1957 [Boston].

A study of the records of the department of preventive medicine and student health at the University of Wisconsin revealed that over 2,000 students report yearly to the student clinic—an incidence rate averaging 171 cases per 1,000 students in the 6-year period studied. Respiratory infections were the single most important cause of admission to the infirmary, accounting for almost 33% of all admissions. The months of highest incidence were January, February, and March. Nonbacterial respiratory infections outnumbered bacterial infections by 5 to 1 and were responsible for about 84% of all respiratory illness. A diagnosis of infectious mononucleosis was made in 21.5% of all the patients with respiratory diseases.

A study of the causation of acute respiratory disease in 290 university students ill enough to be admitted to the infirmary was made with the use of serologic techniques and HeLa-cell cultures for isolation. Known infections thus established included adenovirus in 2%, streptococcic tonsillitis and pharingitis in 8.3%, influenza in 3.4%, herpetic infections in 1.3%, bacterial pneumonia in 1.6%, and psittacosis in 0.3%. The cause of the respiratory disease thus was unknown in 83.1% of the 290 students. A diagnosis of an adenovirus infection could not be made on clinical grounds. Viruses of types 1, 3, and 4 were isolated. Present evidence does not warrant immunization against adenovirus infections in such university students. More data must be obtained for intelligent use of the vaccine in any civilian group. Patients with streptococcic throat infections should receive penicillin therapy for 10 days to eradicate the organism and prevent rheumatic fever. Antibiotic therapy of nonbacterial pharyngitis and tonsillitis is of no advantage and presents the hazards of toxicity or sensitization to penicillin or both.

**Symptomatology of Congenital Pulmonary Arteriovenous Fistula.** F. Grosse-Brockhoff, F. Loogen and H. Vieten. Deutsche med. Wchnschr. **82**:134-137 (Jan. 25) 1957 (In German) [Stuttgart, Germany].

The authors discuss the symptoms and signs of arteriovenous fistulas of the lung on the basis of observations of 9 patients with the congenital form of this disorder and of 1 patient in whom the fistula was probably of traumatic origin but who had symptoms similar to those of patients with the congenital form. The 9 patients with congenital pulmonary arteriovenous fistulas were found among about 2,500 with congenital angiocardiopathies. This pulmonary vascular anomaly is associated in some patients with a hardly detectable cyanosis, whereas in other patients the cyanosis is severe. Anemia may be observed in some patients either as the result of hemorrhages from the lung or from mucosal telangiectases, and these conditions may obscure the existing cyanosis. The great variability in the symptoms is illustrated by the fact that not one of them was present in all 10 patients. Foci of increased density in the roentgenogram of the chest in association with the typical murmur caused by the fistula are the most important diagnostic features. An erroneous diagnosis of tuberculosis may be made particularly if the fistula is located in the upper part of the lung. Conversely, coexistent tuberculosis may make it more difficult to recognize an additional arteriovenous fistula. Confusion with tuberculosis may occur whether there is a hemangioma-like anomaly or a well-defined direct fistula between artery and vein. Auscultation may reveal no abnormality. If the fistula is near the hilus, the roentgenogram of the lung may be normal. It is demonstrated on the basis of a case history that in such cases the diagnosis can be established only by catheterization of the heart and by angiocardiography.

**Bronchial Asthma Treated with Phenylbutazone.** P. Dell'Aera. Riforma med. **71**:97-103 (Jan. 26) 1957 (In Italian) [Naples].

The author reports on the results obtained in 3 groups of asthmatic patients treated with phenylbutazone. The 1st group was composed of 28 patients with bronchial asthma and emphysema but good cardiovascular condition. The 2nd group was composed of 2 patients with asthmatic bronchitis, marked emphysema, and cardiocirculatory insufficiency. The 3rd group consisted of 20 patients, most of them young, with allergic asthma. All patients received 0.3 Gm. of phenylbutazone injected intramuscularly every 12 hours. Other antiasthmatic drugs were not given. An examination made 3 to 4 months after the

treatment showed that the treatment was most beneficial to the patients of the 1st group; 16 patients had recovered completely, 10 had had some attacks but not as severe as those they had had before the treatment; the therapy failed in 2 patients. The results obtained in the patients of the 3rd group were satisfactory. The therapy had to be discontinued because of intolerance in the patients of the 2nd group. Gastric disturbances occurred in 15, suppression of urination with a slight increase of blood sodium and chlorine levels in 3, and kidney disturbances in 5.

**Confusing the Issue: Psychoses as Symptoms of Cancer.** T. H. Howell. Practitioner **178**:233 (Feb.) 1957 [London].

Amid the senile and demented elderly patients there are some whose mental symptoms cloak bodily disease and confuse the issue until a postmortem examination establishes the diagnosis. A recent series of autopsies revealed a group of patients with cancer whose obvious mental symptoms had only made confusion worse. Their histories illustrate some of the peculiar problems in geriatrics. The 6 patients whose case histories are briefly presented were all between 80 and 90 years of age. Most of them were noncooperative and difficult to examine. It is important to realize that in older persons with a new growth mental confusion can be the chief presenting symptom.

**Alcohol-Induced Pain Due to Carcinoma.** A. H. James, H. R. S. Harley, E. H. Horton and F. K. Storring. Lancet **1**:299-301 (Feb. 9) 1957 [London].

Although several workers have reported the occurrence of pain after the taking of alcohol in some patients with Hodgkin's disease, this phenomenon does not seem to have been reported in the presence of other neoplasms. The authors present the histories of 2 patients with alcohol-induced pain due to carcinoma. The 1st patient was a 47-year-old woman first seen in October, 1954. She described attacks of pain behind the upper part of the sternum after taking alcohol. The 1st had been at Christmas, 1952, about five minutes after drinking three-quarters of a glass of port. After a minute or 2 the pain became severe, and radiated around the root of the neck to the back and down both arms. It subsided in about 20 minutes, but soreness persisted until the next day. Between that occasion and her attendance at the hospital in October, 1954, she had taken alcohol 5 times, and each drink had caused an attack of pain identical with the 1st. Roentgenograms showed a round opacity in the anterosuperior portion of the mediastinum. The administration of alcohol by gastric tube or by vein produced the attacks of pain similar to those of which she complained. The mediastinum was not explored because the tumor was presumed to be a manifestation of Hodgkin's disease. A roentgenogram of the chest in March, 1956, revealed that the tumor was larger and better defined. The administration of alcohol at this time (20 ml. by stomach tube) caused only slight discomfort. Later there was no pain after drinking 80 ml. of gin.

Uncertainty about the nature of the tumor led to exploration. A hard mass was found infiltrating the front of the pericardium as well as the superior mediastinal structures behind the manubrium. A globular extension of this mass on each side invaded the anterior margins of the two lungs. The extension of the tumor that had invaded the right lung was resected, but the mediastinal part of the mass could not be removed. The histological appearances of the tumor varied greatly in the sections examined. Follicular collections of small round cells with abortive Hassall's corpuscles suggested that the tumor was of thymic origin as did the appearances at operation. That the susceptibility to alcohol-induced pain disappeared while the tumor was enlarging has not been described before.

The 2nd patient had been well until 2 months before she was hospitalized. At that time she noticed aching across the front of her chest, gradually extending to her back, shoulders, and arms, her whole chest feeling "stiff and taut." These symptoms persisted and became steadily worse. About 2 weeks after her pain started she noticed that alcohol, in the form of beer, stout, or wine, increased the severity of the pain. For 4 weeks she had preferred to abstain rather than experience the acute exacerbation of pain that alcohol always caused. The woman's condition became worse, and she died 13 days after admission. Autopsy revealed a tumor infiltrating the pericardial sac and the left main bronchus and areas of growth in the left lung and in the pancreas, the tail of which was undergoing necrosis; small deposits of adenocarcinoma were found in the kidney. Before concluding that alcohol-induced pain may occasionally be produced by any type of malignant tissue, the authors make 2 reservations. In case 1 the tumor was probably of thymic origin. Thomson has suggested that Hodgkin's disease is a disseminated carcinoma of which the primary growth is in the thymus. Alcohol-induced pain in a patient with a thymic carcinoma might be held to support this hypothesis. The 2nd patient had an adenocarcinoma, probably of pancreatic origin. Alcoholism is among the recognized causes of acute pancreatitis.

**Studies on Anti-V: A Recently Discovered Rh Antibody.** E. R. Giblet, J. Chase and A. G. Motulsky. J. Lab. & Clin. Med. **49**:433-439 (March) 1957 [St. Louis].

The new blood group antibody, "anti-V," recently described by DeNatale and co-workers (THE JOURNAL **159**:247 [Sept. 24] 1955) was found in the serum of 2 previously transfused patients. The 1st patient was an elderly white man with severe hematuria and anemia. His history included a leg amputation 10 years previously, with subsequent complications requiring the transfusion of 22 units of blood, several of which were Rh positive. When admitted to hospital he received 8 units of blood, but death occurred rapidly. It was because of difficulties observed in cross-matching that his blood was studied. His erythrocytes were group A; the Rh genotype was R'r (Cde/cde). His serum contained both anti-D and anti-V. The 2nd patient, a young white man with congenital nonspherocytic hemolytic anemia, was found

on routine serologic study to have anti-D and anti-V in his serum. His sensitization had occurred 12 years previously when he received 10 units of blood after a war injury. Blood drawn from this patient was the source of anti-V used for studies concerning the racial distribution of the V antigen and its relation to the Rh blood group system, and for additional studies concerning the incidence, serologic nature, and destructive capacity of anti-V in vivo.

Racial studies confirmed the previously reported high incidence of the V antigen in Negroes and its rare occurrence in white persons. The antigen was also found to be unusual in orientals (Japanese or Filipinos) and American Indians. Further confirmation was obtained for the hypothesis that the V gene is present only in chromosomes with the Rh genes c and e. The occurrence of V with cDe is apparently more frequent than with cde. The ability of the new blood group antibody to destroy erythrocytes in vivo was shown in the younger of the 2 patients. It might, therefore, be responsible for hemolytic transfusion reactions. The fact that the 3 examples of anti-V so far discovered—in the patient reported on by De-Natale and in the authors' 2 patients—have occurred in Rh(D)-negative persons is contrary to expectation and would appear to be more than coincidental. Assuming that the only factor preventing the possible formation of anti-V is the presence of the V antigen, by far the most numerous candidates for making this antibody should be Rh-positive, V-negative recipients of Rh-positive, V-positive blood. No such examples have been found. To explain this discrepancy, at least 2 possibilities may be considered. First, the V antigen, like C, may rarely cause an antibody response in Rh(D)-positive recipients. If this were true, one would expect to find the antibody in those Rh-negative, V-negative persons who had been sensitized by the relatively uncommon blood from an Rh-negative, V-positive donor or by the more common blood from an Rh-positive, V-positive donor; the latter probably was the case in the authors' 2 patients. A 2nd possibility is that anti-V has been found in the blood of Rh-positive persons but not recognized as such. To reveal the presence of anti-V it would be necessary to absorb the serum with rr (cdef/cdef) V-negative cells, but studies of this type have not yet been carried out.

**Frequency of Partial Megaloblastic Erythropoiesis in Older Achylic Patients with Slight Anemia: Iron, $B_{12}$ and Vitamin C Content in Blood: Dimorphic Anemia, Anemia with Multiform Pathogenesis, and Iron Treatment: Diagnostic Significance.** J. Pedersen, J. Lund, A. S. Ohlsen and H. P. Ø. Kristiansen. Ugesk. læger 119:1-14 (Jan. 3) 1957 (In Danish) [Copenhagen].

Consecutive examinations in 1955 of the bone marrow in 46 patients, aged at least 50 years, with achylia refractory to histamine, slight anemia but otherwise no certain signs of pernicious anemia revealed beginning or partial megaloblastic erythropoiesis in 7. Comparison of the hematological data in 10 patients with partial megaloblastic erythropoiesis and 10 patients with achylia, total megaloblastic erythropoiesis, and marked anemia showed that, while the iron and vitamin C deficiency seemed to be equally marked in the 2 groups, the vitamin $B_{12}$ deficiency was less in the 1st group. The patients in this group seem to represent 2 clinical types, 1 with a beginning pernicious anemia complicated by iron and vitamin C deficiency, the other marked by anemia of other pathogenesis, most often a chronic nephrogenic hemolytic anemia intermittently complicated by toxic-infectious anemia due to medicamental intoxication and colibacteremia. Diagnosis of megaloblastic erythropoiesis was made only when megaloblasts of classic type were observed. Their appearance can apparently be accelerated by overcoming a present iron deficiency. Intensive iron therapy was accordingly applied in cases in which diagnosis was uncertain, and diagnosis of megaloblastic erythropoiesis was made in this way in 3 cases. Characteristic changes in the leukopoiesis, including macrometamyelocytes, can sometimes be seen in the marrow when typical megaloblasts are not yet present. Examination of the sternal marrow is the most important method for establishing the diagnosis of partial megaloblastic erythropoiesis. Treatment with vitamin $B_{12}$, iron, and vitamin C is beneficial but must be applied intensively; this is particularly true of iron, which must often be given intravenously at the start. In uncomplicated cases normal blood values will often not be attained until after 6 months' treatment. Iron deficiency in patients with partial megaloblastic erythropoiesis is ascribed not only to reduced resorptive ability but also to insufficient nutrition. Presumably, older women with achylia are especially likely to be inadequately nourished.

## SURGERY

**Vagal Resection in Treatment of Duodenal Ulcer.** A. A. MacKelvie. Brit. M. J. 1:321-323 (Feb. 9) 1957 [London].

Of 473 patients (401 male and 72 female) between the ages of 10 and 79 years with duodenal ulcer, 118 underwent vagal resection alone, 332 vagal resection with gastroenterostomy, 19 vagal resection and pyloroplasty, and 4 vagal crush. Of the 118 patients, 3 died —1 from anesthesia, 1 from secondary renal carcinoma, and 1 from aneurysm, and 10 were lost to follow-up. Twenty-three of the remaining 105 patients required gastroenterostomy for symptoms secondary to vagal resection, such as gross gastric retention, with foul flatulence and diarrhea. Six additional patients were awaiting gastroenterostomy. Vagal resection alone, although it appeared complete, thus was a failure in 28% of the 105 patients. Recurrence of duodenal ulcer occurred in 4 of the remaining 76 patients, and many others had flatulence, diarrhea, and uncomfortable fulness after meals. Nine of the 332 whose primary operation consisted of vagal resection and gastroenterostomy died of the operation, an operative mortality of 2.7%. Of the remaining 323, 7 died of intercurrent disease unrelated to the operation or ulcer and were free of dyspepsia to the date of death. Ten were symptom-free, but they had been followed up for less than 1 year after the operation. Eight patients were lost to follow-up. Of the remaining 298, 238 (group 1) had

no gastric symptoms, 31 (group 2) had very minor symptoms, 8 (group 3) had symptoms that were not preventable but which did not interfere with their activities, 13 (group 4) had symptoms preventing full enjoyment of life, and 8 (group 5) were therapeutic failures. The 277 patients in the first 3 groups were well satisfied, they were no longer on a diet, and most of them had returned to their preoperative occupations.

The 4 patients in whom vagal crush was done were therapeutic failures. Excellent results were obtained in the 14 patients with vagal resection and pyloroplasty. Operations on the vagal nerves alone, either by resection or by crushing, do not give good results in patients with duodenal ulcer. Excellent results are obtained with vagal resection combined with posterior gastroenterostomy in more than 90% of the patients. Equally good results may be obtained by vagal resection combined with pyloroplasty. The results are at least as good as those after partial gastrectomy, and the operative mortality is probably appreciably lower. These good results, added to the fact that partial gastrectomy is not excluded as a further possible operative treatment for failure in resistant cases, indicate that the combined operation should be the method of first choice in the treatment of patients with duodenal ulcer.

**Arteriovenous Fistulas in Young Patients with Chronic Obliterating Arteriopathies.** G. Cadili. Minerva chir. 11:1121-1131 (Nov. 30) 1956 (In Italian) [Turin, Italy].

A group of 143 patients with chronic obliterating arteriopathies were subjected to combined operation (gangliectomy, splanchnicectomy, hemiadrenalectomy, and in some arteriectomy) and/or to treatment with a "lytic cocktail," which in many patients made it possible to avoid or postpone operation. Four to 8 years after the treatment most of the patients were still well; some had a relapse after from 1 to 3 years; and 13 patients had a relapse with pain more severe than before the treatment after a period of from 1 to 12 months. Arteriovenous fistulas were found in the vascular bed of the diseased limb of 9 of these 13 patients. High concentration of oxygen was found in the diseased venous trunks. Arteriography helped to locate these trunks, but the authors warn that arteriography may give negative results if, because of location, size, and spasm, the contrast medium cannot reach the fistulas. The authors believe that the fistulas were the cause of the relapse. Hemodynamic alterations that interfered with the nutrition of the peripheral zones were also present. Amputation of the diseased limb is the only treatment from which these patients can derive permanent benefits.

**Emergency Definitive One-Stage Surgery for Intestinal Obstruction.** W. H. Ferguson and W. W. Chase. M. Ann. District of Columbia 26:61-67 (Feb.) 1957 [Washington, D. C.].

The authors began to treat acute intestinal obstruction by a 1-stage definitive operation in 1954 and so far have used this method in 45 patients, including 19 with lesions of the small and 26 with lesions of the large intestine. They describe the surgical technique for the small intestine and for the ascending and descending colon, pointing out that surgical decompression of the acutely obstructed colon as well as of the small intestine is a safe and necessary procedure. In the hands of a skilled surgeon with modern hospital facilities there should be no need for special equipment or training. A through-and-through cotton suture produces an anastomosis that is secure and capable of early function in the small as well as in the large intestine.

The following are important aids in management: attention to the fluid and electrolyte requirements, preoperative sigmoidoscopic examination, ready availability of a barium enema (no barium should be given by mouth if obstruction is suspected), preoperative introduction of a tube for gastric suction, endotracheal anesthesia, if possible, removal of contaminated tissues and instruments from the operative field, avoidance of intestinal spillage into the peritoneal cavity; changing of gloves and drapes after the anastomosis, introduction of neomycin into the intestinal lumen and the peritoneal cavity, use of through-and-through wire suture if there is doubt about the security of the wound, postoperative dilation of the anal sphincter, giving of neomycin through the gastric tube on the day after the operation, and supportive antibiotic therapy. After gas is passed by rectum a regular diet can be started. Of the 6 deaths that occurred, 5 were due to medical rather than surgical complications. The average stay in the hospital were 10 to 11 days, and normal intestinal function was usually present on the third postoperative day. The authors believe that a shorter hospital stay and 1 trip to the operating room are far less demanding in both time and risk than multiple procedures.

**Surgical Treatment of Nontumorous Temporal Lobe Epilepsy.** J. E. Paillas and P. Pruvot. Presse méd. 65:197-199 (Feb. 2) 1957 (In French) [Paris].

Of 45 patients with psychomotor epilepsy who were subjected to total temporal lobectomy and followed up postoperatively for from 1 to 7 years, 13 made a complete recovery with complete freedom from attacks. At least 75% improvement with a decrease in the number and severity of the seizures occurred in 11 patients. The remaining 21 were therapeutic failures in that the number of their seizures remained unchanged or that they were improved by less than 75%. Of 37 patients who had personality disorders before the operation 18 were improved. This applied particularly to patients with violent compulsions while those with delusions of persecution and with ideas of revenge were not benefited. Of 8 patients with impotence or frigidity, 2 showed great improvement. The encephalograms of 19 patients revealed disappearance of irritative discharges with tracings within normal limits. Nonirritative discharges (delta and theta waves) persisted in the electroencephalograms of 10 patients. The abnormal tracings in the preoperative encephalograms remained unchanged in the postoperative encephalograms of 16 patients.

Of 14 patients in whom the temporal lobe epilepsy was secondary to fetal dystocia, trauma, or otomastoid infections, 5 made a complete recovery, 7 were improved, and only 2 were therapeutic failures. These data suggest that a definitely known causative factor may be a valuable aid in prognosis. Of 27 patients with a history of grand mal, 14 made a complete recovery or were improved and 13 were therapeutic failures. A history of grand mal does not seem to be a definite contraindication to lobectomy. Thirteen of the 45 patients had preoperative neurological signs, such as hemiplegia, hemianopsia, or contralateral sensory disturbances; 8 of these 13 patients were therapeutic failures. Lobectomy seems, therefore, to be of doubtful value in patients with neurological signs, and a hemispherectomy may be preferable. Of the encephalograms of the 45 patients, those of 37 patients showed unilateral seizure discharges and those of 8 patients bilateral seizure discharges. Of these 8 patients, 2 underwent bilateral lobectomy and were therapeutic failures. Unilateral lobectomy was performed at the site of the most severe abnormality in the other 6 patients, 2 of whom were improved and 4 of whom were failures. These data confirm the unfavorable prognosis of surgical treatment of epilepsy associated with bilateral abnormal encephalograms. Of 14 patients in whom pneumoencephalography revealed a cerebral atrophy manifested by a dilation or a unilateral ventricular or localized adhesion of the inferior horn, 5 made a complete recovery, 5 were improved, and 4 were therapeutic failures. The radiologic detection of anatomic lesions may be of valuable aid in the operative prognosis.

Total frontal lobectomy is associated with a minimum of sequelae and has a favorable effect on the seizures and personality disorders in patients with severe psychomotor epilepsy that is refractory to drug therapy. Total frontal lobectomy, however, should be performed only in patients carefully selected with the aid of electroencephalography and radiology and according to the clinical appearance. The chances for success are best in patients with epilepsy of dystocic or traumatic origin, with a unilateral circumscribed electroencephalographic focus and with radiologic abnormalities that are characteristic of anatomic lesions or of atrophy limited to the temporal lobe.

**Acute Ileitis with Ulceration and Perforation Due to Paratyphoid Fever: Report of Eighty-five Cases.** J. V. Conroy. Mil. Med. **120**:79-91 (Feb.) 1957 [Washington, D. C.].

Eighty-five of 203 North Korean prisoners of war with ileal perforation or ulceration due to paratyphoid were operated on. The mortality rate was 22% for all patients and none for those who had surgical repair within 2 days of their perforation. In most patients a resection of the ileum with end-to-end anastomosis was performed. Sixty-seven patients had single perforation and 13 multiple perforations of the ileum and 5 had ulceration without perforation. The ileum was dilated, thickened, and covered with a brown exudate and with external evidence of peritonitis. All ulcers were transverse and on the antimesenteric border. Their depth varied from minimal penetration to perforation. The number of ulcers was 1 to 9 in a single resected specimen. Acute perforation of the ileum and peritonitis are a much more common complication of paratyphoid, than was previously believed. It may be the presenting syndrome of the disease. Roentgenograms of the abdomen are a valuable aid in the diagnosis. Cultures of the blood, ileal ulcers, and stool should be made in all patients to determine, if an enteric pathogen is the causative agent. Operation is the treatment of choice for these patients.

**Osteoradionecrosis of the Mandible.** J. Gaisford and F. Rueckert. Plast. & Reconstruct. Surg. **18**:436-447 (Dec.) 1956 [Baltimore].

Necrosis of the mandible after radiation therapy has been a serious and not infrequent complication ever since this form of treatment was introduced at the turn of the century. The authors report their experience in the management of 54 patients with this problem in the past 7 years. Most observers believe that necrosis of the mandible is produced by a combination of heavy irradiation, infection, and trauma. The mandible, because of its ribbonlike shape, compact composition and presence of but a single nutrient artery on each side, is even more susceptible to the effects of irradiation than the other compact bones in the head. Radionecrosis of the mandible may result from x-ray treatment through the jaw aimed at a primary lesion elsewhere in the oral cavity, but usually a cancericidal dose of x-ray for a carcinoma of the mandible itself will result in necrosis of the jaw. In the early stages of radionecrosis of the mandible there may be only dental symptoms—hypersensitivity of the teeth, continuous dull toothache, and cavities. In the late stages symptoms are severe and constant. There is probably no lesion about the head and neck that makes a patient as miserable as this condition. There is marked trismus, continuous prolonged pain not responding to the usual narcotics, a foul-smelling mouth, and, if there is soft tissue necrosis, there may be a draining orocutaneous fistula. Patients with this disease usually have difficulty eating because of the pain and inability to open the jaws. As a result they are malnourished, sometimes to the point of starvation.

Sixteen of the 54 patients were treated conservatively because their conditions were considered inoperable. These all died with uncontrolled tumor. Seventeen of the 38 patients in whom resection was performed were found to have necrosis only. Twenty of 38 patients subjected to resection died: 7 as the result of hemorrhage from the carotid artery, 6 from tumor and necrosis, 5 from other unrelated causes, and 2 from necrosis only. When last seen 18 of the patients were alive without tumor. The longest survival to date is 7 years, the shortest 3 months. Radionecrosis of the mandible and of the adjacent skin is a serious complication, and the authors believe that in most cases it could have been prevented. Prompt resection of the necrotic mandible and primary closure of the involved tissues offers the best opportunity for a good result. Where primary closure is not possible, reconstruction should be by pedicle flaps.

Free skin grafts do not do well when placed over heavily irradiated tissues of the face and neck. Jaw reconstruction is not considered necessary for most patients operated on for necrosis of the mandible. The surgical risk in this type of case should be negligible. Even patients with a few months life expectancy are candidates for surgical treatment because of the palliative results.

**Cancer of Palate: Clinical Study.** J. Fairbanks Barbosa and J. B. da Silva Netto. Rev. paulista med. 49:191-210 (Sept.) 1956 (In Portuguese) [São Paulo, Brazil].

Thirty patients of both sexes with cancer of the palate were observed. Most of the patients were between the ages of 50 and 60 years. The tumors were squamous cell carcinoma in 25 patients and glandular tumors (mixed tumors, cylindromas, or adenocarcinomas) in five. A causal factor found in several patients was the callosity formed by a prosthesis. The most frequent forms of squamous cell carcinoma were those marked by superficial, destructive, infiltrating, or vegetating ulceration. Glandular tumors appeared as submucous nodules that underwent ulceration and malignant degeneration and caused destruction of the skeletal bones and diffused to nearby structures. The diagnosis of the size of glandular tumors was made by roentgenographic examination. Malignant glandular tumors of the palate followed a rapid course. The prognosis, when the tumors reached the retromolar region, the uvula, or the region of the tonsils or when they perforated the palate and invaded the regions of the nasal fossae, the facial sinuses, or the zygomatic fossa, was poor. Tuberculous ulceration and malignant granuloma were the main conditions to be ruled out. Carcinoma without involvement of the bones and lymphomas were treated with x-rays. Those with involvement of the bones and those resistant to roentgenotherapy were excised. Glandular tumors were treated by operation followed by roentgenotherapy. In the cases reported most of the patients complained of rapid loss of weight. Malignant tumors diffused to the alveolar bones in 8 cases, to the tonsillar region in 8, to the nasal fossae and facial sinuses in 2, and to the pharynx in 1. There was no propagation of the tumor in 11 cases. Metastases, either unilateral or bilateral, in the cervical lymph nodes occurred in 14 patients. Resection of the metastatic lymph nodes was performed in 5 patients. Neoplastic nodes were found on histological examination in the resected material of 4 of the 5 patients. No conclusions were drawn by the authors because the follow-up period was only 2½ years.

**The Treatment of Diabetic Arteritis of the Lower Limbs.** M. M. Plauchu. J. méd. Lyon 38:113-124 (Feb. 5) 1957 (In French) [Lyon, France].

Arteritis is 11 times more frequent in diabetics than in normal persons. The frequency is high among patients who have had diabetes for more than 5 years. The author found that of a group of 211 diabetic patients 45 had arteritis. Arteritis occurred in 10% of those who had had diabetes for less than 5 years, in 10% of those who had had diabetes for 5 to 15 years, and in 40% of those who had had diabetes for more than 15 years. No direct relationship between the frequency of arteritis and the fact that the patients had been treated with insulin was found. Obesity and superalimentation should be considered only as predisposing factors. Of 45 patients with arteritis, 17 were obese and 27 had retinal lesions. Latent diabetic arteritis was the most frequent form observed. It was located in the upper limbs only in 2 patients. Good control of the diabetes, use of iodides, and a diet poor in lipids are advised by the author for the treatment of latent diabetic arteritis. Diabetic arteritis not complicated by gangrene may persist for several years. Intermittent claudication was the first symptom in 11 of 19 patients with arteritis. The authors advise control of the glycosuria and maintenance of a normal blood sugar level. Intra-arterial and intrathecal injections are preferred to treatment with vasodilators. Physiotherapy should be considered only as a secondary type of treatment. Periarterial and lumbar sympathectomy are of some help. Seventeen of the 45 patients with arteritis had gangrene. Diabetic coma in patients with gangrene is rare, it occurred in only 1 of the 17 patients. Lowering the blood sugar level and intra-arterial injections of procaine, heparin, and penicillin constitute the best treatment for patients with gangrene. Amputation performed at a sufficiently high point is still the only treatment for patients with massive gangrene. In such patients the prognosis is poor.

**The Plastic Replacement of Severed Flexor Tendons of the Fingers.** T. L. Sarkin. Brit. J. Surg. 44:232-240 (Nov.) 1956 [Bristol, England].

The occurrence of an injury involving the flexor tendons of the finger within the digital theca is a calamity. At best the treatment is prolonged and complicated, and many patients never recover a functioning finger. The technique that is now generally accepted as giving the most consistently satisfactory results is the transplantation, with a free tendon-graft, of the cut flexor digitorum profundus tendon from the palm of the hand to the distal phalanx, and the complete removal of the flexor digitorum sublimis tendon in this area. Free grafting of the profundus tendon requires special skill, experience, and great care. Even experts occasionally fail to obtain satisfactory results. Other disadvantages of this method are the length of time required for rehabilitation during which supervision and physiotherapy, together with the cooperation and willingness of the patient, are necessary and the fact that the effective treatment of a divided profundus tendon requires the presence of a normally functioning sublimis unit. The key to success in tendon repair lies to a large extent in the total avoidance of adhesions around the tendon. A technique is described and illustrated in detail whereby severed flexor tendons in the digital theca are replaced by a double length of adequate strength nylon covered by polythene tubing, which is inserted as a functioning unit between the distal phalanx, through which it is passed, and a profundus tendon at the

wrist, to which it is firmly sutured, passing through the tendon-sheath en route from the finger to the wrist.

The possible disadvantages and difficulties of the technique are discussed, namely the questions of the strength of the plastic and of the junctions between it and the phalanx distally and the tendon proximally and its inertness in the body. The evaluation of the late clinical results will require more time. The principle of artificial tendons might eventually be extended to the field of tendon transplantations and the rehabilitation of the paralyzed. If artificial tendons can function along anatomic pathways, there appears to be no reason why they should not function along artificial pathways. Often a tendon transplantation is not practicable due to the anatomic lack of a suitable nearby tendon. If this limitation is removed, there is no theoretical reason why a suitable muscle far removed from the paralyzed area should not provide the motor power to that area via a long artificial tendon.

**Treatment of Angiomas**. R. W. O'Brien. Plast. & Reconstruct. Surg. **18**:448-459 (Dec.) 1956 [Baltimore].

The multiplicity of names applied to angiomas has led to confusion, but they may be grouped into 2 broad categories, namely the capillary and the cavernous. Capillary hemangiomas include the port-wine stain or nevus flammeus and the strawberry birthmark or hemangioma simplex. The cavernous angiomas are soft compressible tumors consisting of large thin-walled sinuses with little intervening stroma. They may produce pronounced enlargement of the cheek, nose, ears, lips, and other facial structures and may interfere seriously with function. They often produce blue discoloration of the overlying skin, indicating a predominant venous component. Phleboliths often develop within them. Cirsoid aneurysms are related closely to cavernous angiomas and in fact may be cavernous angiomas with single or multiple arteriovenous fistulas. Spontaneous regression occurs frequently but not invariably in hemangioma simplex, but spontaneous regression is not observed in the port-wine and cavernous angiomas. The relative ease with which these lesions can be treated in an early stage and the great difficulty of restoring normal or near normal appearance, even after spontaneous regression, when involvement is extensive make it necessary to treat them when they are still small. Accordingly, it appears to be highly illogical to adopt an expectant attitude, as some have proposed. In addition to progressive growth, these lesions may ulcerate, become infected, and give rise to profuse, and at times fatal, hemorrhage.

Except when growth, pressure, or hemorrhage is producing imminent danger, the treatment of these lesions is not an emergency. Therefore, it behooves the physician or surgeon never to use a method of treatment that may endanger life or produce greater disfigurement or dysfunction than is likely to result from nontreatment. Surgical excision of both capillary and cavernous hemangiomas is being resorted to more and more, as it is safer and produces fewer complications than do other methods of treatment, and it gives satisfactory cosmetic results. When irradiation is used, extreme care must be taken in evaluating the dosage. Cavernous hemangiomas whose situation and extent render excision inadvisable are best treated by means of injection of sclerosing solutions, by electrocoagulation or by a combination of these methods.

**Biliary Ileus**. R. Mosimann. Helvet. chir. acta **23**:496-512 (Dec.) 1956 (In French) [Basel, Switzerland].

Thirteen of more than 200 patients with intestinal obstruction and 450 with gallstones were found at operation to have biliary ileus. Three of the 13 died, and 1 required a 2nd operation because of duodenal stenosis. Spasm, parietal edema, and localized enteritis were frequent symptoms. The latter caused necrosis and intestinal perforation in 1 patient. Ten patients had pain in the right hypochondrium. Visible calculus in the terminal part of the dilated intestine was the most reliable roentgenologic finding. Presence of gas or of some contrast medium in the bile ducts was another significant roentgenologic finding. A median incision below and above the navel permitted exploration of the intestine in its entire length. Transverse or longitudinal enterotomy was performed and transverse absorbable surgical sutures were placed in 3 layers continuously after clamping of the intestine. Palpation of the gallbladder often fails to reveal the calculus because of its close adherence to the liver. Great caution is required in making the dissection in order to avoid perforating the intestine or the gallbladder. This accident makes cholecystectomy inevitable and greatly aggravates the situation. Some biliary-intestinal fistulas close spontaneously and do not cause any more trouble. In 1 patient such a fistula caused an intestinal stenosis. Laparotomy showed in this patient that a band of adhesions had constricted the lumen of the duodenum. Except for one patient who was observed 2 years after the operation, the authors were unable to make roentgenologic examinations to find out what had happened to the fistulas. Biliary-intestinal fistulas should be left intact during the 1st operation for biliary ileus and repaired later. An exception to this rule should be made only in case of duodenal stenosis or in presence of clinically observable cholangitis.

**Traumatic Pneumopericardium: Case**. F. Rosa and H. Coardeza. Arch. urug. med. **49**:80-90 (July-Aug.-Sept.) 1956 (In Spanish) [Montevideo, Uruguay].

Traumatic pneumopericardium is rare. When pneumopericardium is due to associated lesions of intrathoracic and intraperitoneal structures, the diagnosis is difficult and the prognosis is serious. The subject of this report was a child 4-years-old who was brought to the hospital immediately after he had suffered a wound in the chest by a firearm. The patient was vomiting food and blood at repeated intervals, but not constantly. The clinical symptoms were those of perforation of an abdominal viscus. The patient had no shock. The roentgenogram of the chest and a lateral teleroentgenogram showed a pneumopericardium as a transparent band of air within the cardiac shadow. The operation was done immediately with the patient

under general anesthesia. It showed wounds in (1) the diaphragm (2) the left posterior lobe of the liver, and (3) the lesser curvature of the stomach. The operation consisted of suture of wounds, leaving a peritoneal drain. The postoperative course was uneventful; there was rapid recovery without sequels. Clinical, roentgen and electrocardiographic follow-up showed permanent cure of the patient.

**Hemolytic Transfusion Reaction with Fatal Outcome Due to Rare Blood Type Antibody (Anti-C).** B. Barfod and G. Munk-Andersen. Ugesk. læger **119**:37-40 (Jan. 10) 1957 (In Danish) [Copenhagen].

The fatal hemolytic transfusion reaction reported was due to an Rh undertype antibody, anti-C. The presence of another rare blood type antibody of immune character, anti-Jk$^a$, was demonstrated 1 week after the transfusion. The authors discuss performance of compatibility tests that can establish antibodies outside of the ABO system, especially in the case of recipients who have previously been exposed to an immunization either by blood transfusion or by pregnancy. As increasing application of transfusions will bring about more frequent immunization of the patients, with consequent increasing risk of transfusion complications, blood transfusions should be prescribed only on well-considered indications.

## NEUROLOGY & PSYCHIATRY

**The Outcome of Patients with Herpes Zoster.** J. M. de Moragas and R. R. Kierland. A. M. A. Arch. Dermat. **75**:193-196 (Feb.) 1957 [Chicago].

Generally herpes zoster resolves without complication, but in some patients it produces complications or sequelae that may incapacitate the patient. The most important among these is postherpetic neuralgia. The authors analyze some of the factors that determine the severity of the disease. They attempt to outline its natural course and to provide a "base line" useful in determining the results of treatment. The records of 916 patients seen at the Mayo Clinic between 1935 and 1949, inclusive, with the diagnosis of herpes zoster or postherpetic neuralgia were reviewed. Sex distribution was essentially even. Study of the patients was undertaken by groups divided by ages in decades. Duration of the postherpetic neuralgia was used as an index of the severity of the process. It was found that the incidence of herpes zoster increased with age, from 24 in patients in the age group under 20 years to 270 in patients in their 60's. The group aged 70 years or more included 160 patients, absolutely a smaller number but actually larger, considering the relatively smaller percentage of population in this age group.

Postherpetic neuralgia likewise showed a relationship to the ages of the patients. As the age increased, the number of patients without pain diminished from 83.3% in the age group under 20 years to 8.7% in the age group of 70 years or more. Simultaneously, the duration and severity of the postherpetic neuralgia increased. Trigeminal location of the herpes zoster was observed in 149 patients (16.3% of the total). The postherpetic neuralgia was of longer duration in this group than in the entire series. Also this group was more prone to have severe complications during the acute phase of the disease. Enucleation of the eye was done in 2 patients, owing to perforation of the cornea and to absolute glaucoma. The different age groups received the same type of treatment during the acute phase of the disease. Acetylsalicylic acid, autohemotherapy, and roentgenotherapy were the more widely used. To relieve postherpetic neuralgia, roentgenotherapy, cobra venom, posterior pituitary extract, Protamide (a proteolytic enzyme preparation), and vitamin $B_1$ and $B_{12}$ were given to most of the patients. Infiltration of procaine hydrochloride, which was performed in 14 patients, helped 2. Infiltration of alcohol, which was performed in 23, also helped 2. Avulsion of the nerve, which was performed in 6 was of no value. Rhizotomy was effective in 3 of 8 patients. Treatment of postherpetic neuralgia did not seem to change the slow tendency of the neuralgia to improve with time, but in some instances, fortunately very seldom, the severity of pain was stationary or even progressive. Age and localization (trigeminal) seemed to be the decisive factor in the prognosis of herpes zoster.

**Electroencephalographic Study of a Few Cases of Hepatic Coma.** R. Cloche. Presse méd. **65**:135-137 (Jan. 23) 1957 (In French) [Paris].

Electroencephalographic examinations were made in 14 patients with neuropsychiatric symptoms associated with severe hepatic insufficiency. Anomalies of a characteristic, ample, and spiking type, presenting a positive component, were observed in 6 patients who were examined during precoma and coma. The tracings varied with the degree of unconsciousness. An evaluation of the blood ammonia level made during coma in 2 patients showed it to be high. No relation was found between this level and the intensity of the coma.

**Treatment of Mental Illness: The Use and Misuse of Sedation and the Seclusion Room.** H. A. Wilmer. California Med. **86**:93-98 (Feb.) 1957 [San Francisco].

A series of 939 patients admitted to the locked receiving ward in the psychiatric service of the U. S. Naval Hospital, Oakland, Calif., over a 10-month period, many of them psychotic and in an acute initial episode, was treated with group therapy, which more appropriately should be called a therapeutic community. The locked ward contained 34 beds in a single room. The concept of the therapeutic community involves free communication among patients, between patients and staff, and among members of the staff. The staff was told in the beginning of this experiment that the use of the quiet room would be discontinued and that sleeping pills were to be given only in unusual circumstances. A formal sick call was held each morning, followed by a ward group meeting lasting about 45 minutes, at which all patients and staff—nurses and corpsmen—were expected to be present. Only 2 of the 939 patients refused to attend the meet-

ings. Both were severely paranoid schizophrenic patients who were overwhelmed by fear. Immediately after the group meeting, the staff met separately to discuss the meeting and ward and staff problems. While the staff was holding its meeting, the patients gathered in a spontaneous group on the ward. At first, the staff doubted whether the ward could be operated without the use of quiet rooms, restraint, and parenteral sedation. Within 2 or 3 months it was obvious that the plan would work and that the best and most humane qualities in staff and patients were brought to the fore.

The routines of the ward were group-oriented, but group therapy as such played only a small part. Group membership was constantly changing, with an average of 3 patients coming and going every day. On the entry of severely sick, new patients, a spontaneous psychodrama was performed. As many as 5 or 10 patients were admitted at one time, some in mechanical restraint and many of them after having spent days or weeks in seclusion rooms in other hospitals. Only about 8% of the first 250 patients admitted received chlorpromazine and reserpine. After 4 months, when it became evident that the social and therapeutic experience of the ward milieu was effective and that its efficacy did not depend on medication, the newer drugs were evaluated. At the end of the 10 months 27.6% of the patients were receiving 1 of these drugs. They were considered to be of particular help in treating the more aggressive, hyperactive psychotic patients and those with delirium tremens. The decline in the use of the quiet room and sedation on the receiving ward, as well as an increase in use of the tranquilizing drugs, coincided with a decrease in use of electroshock and a discontinuance of the use of insulin coma therapy in the hospital. Patients who did not require a locked ward were quickly transferred to the open receiving ward which was established 5 months after this program began. It was possible to greatly diminish the quantity of sleep-inducing drugs and practically to eliminate the parenteral administration of barbiturates. Restraints were never used. To be dealt with in this atmosphere of candor and relative freedom seemed to evoke a responsive attitude in the patient, and many of them benefited from it.

**Dizziness Attacks and Continuous Dizziness in the Aged.** E. J. Orma and M. Koskenoja. Geriatrics. 12:92-100 (Feb.) 1957 [Minneapolis].

This is a 2nd report on dizziness in a group of patients over 64 years of age, who did not represent a random sample of old people with dizziness because the subjects were solicited through newspaper advertising and included a large number of patients with more severe forms of dizziness than would be the case in a random sample. Physical, neurological, otorhinolaryngologic, and ophthalmological examinations, laboratory tests, and roentgenographic studies were made. The authors discussed in an earlier report the postural type of disturbance in equilibrium, which is the most common type of dizziness observed in the aged. A table listing the type of attack of dizziness in the 45 patients reviewed here shows that the attacks were of central neurological origin in about half of the patients, that is, in 12 they were definitely so and in 10 they were probably of this origin. An attack of dizziness was regarded as neurological in origin if other clear neurological symptoms had been associated with it and other causes, especially the otogenous, could be excluded. In the remaining 23 patients, the attacks of dizziness were connected with Ménière's disease, chronic otitis media complicated by labyrinthitis, a labyrinthine vascular accident, agina pectoris, cardiac arrhythmias, laryngeal vertigo, infections, poisoning, agoraphobia, vomiting, and head injury.

The authors define continuous dizziness as a continuous disturbance in equilibrium independent of movement or position. This symptom was observed in only 8 of 112 elderly patients with dizziness. Most of the patients of this group were in poor physical condition. Many had severe ataxia and tremors and poor mental activity. Apparently such continuous dizziness occurs in patients with extensive, diffuse brain lesions, either degenerative or arteriosclerotic.

**The Response of Normal Men to Lysergic Acid Derivatives (Di- and Meno-Ethyl Amides): Correlation of Personality and Drug Reactions.** J. M. von Felsinger, L. Lasagna and H. K. Beecher. J. Clin. & Exper. Psychopath. 17:414-428 (Oct.-Dec.) 1956 [New York].

Lysergic acid diethylamide was given to 10 healthy men and lysergic acid ethylamide to 9 similar persons after psychological interviews and Rorschach tests in an attempt to increase understanding of the psychological and physiological factors involved in psychotic states by reproducing such states with the aid of these drugs in these volunteers. Interviews and Rorschach tests were repeated during the height of the reaction of the volunteers to lysergic acid diethylamide. Total doses of lysergic acid diethylamide varied from 39 to 86 mcg., most persons receiving 1 mcg. per kilogram of body weight. The drug was given orally either in the fasting state or after a light breakfast. The total dose of lysergic acid ethylamide was 0.25 mg. in 3 persons and 0.5 mg. in 6 persons. The drug was given subcutaneously. Both the drugs were administered as unknowns.

The following observations were made in the men who received lysergic acid diethylamide: changes in vital signs were of slight moment; giddiness, tremulousness, and paresthesias were frequent; mood changes included, commonly, tension or anxiety and desire to laugh without cause; less frequently euphoria and erotic sensations were encountered; thought and speech processes were slowed down and efficiency impaired; and perceptual changes or visual illusions were produced in half the persons. After taking the drug 7 of the 10 volunteers showed distinctive changes in the Rorschach test taking the form of an exaggerated caricature of the predrugged state in which weaknesses of ego function were intensified. The degree of change in Rorschach findings and the amount of reaction to the drug were correlated positively with personality disturbances or maladjustment. Observations in the men who were given lysergic

acid ethylamide were as follows: Transient hypertension, tachycardia, tachypnea suggestive of epinephrine release, paresthesias, dizziness, and nausea were frequent. Mental changes were predominantly experienced as dulling of the senses, confusion, shakiness, and apprehension. Four of the 9 volunteers became mildly hostile and paranoid. One other experienced acute panic. As with lysergic acid diethylamide, the degree of drug reaction was positively correlated with personal maladjustment.

The changes produced by these drugs were not striking conversions of normal to psychotic but rather consistent expansive exaggerations of the predrugged personality in which structural weaknesses and immature factors were magnified. In some persons whose personalities are already characterized by pathological signs, such a process may produce a "psychotic" picture. The process itself is better viewed as a release of existing tendencies rather than as a creation of new elements. Problems of control and design are especially difficult in drug experimentation, not to speak of "experimental psychiatry," and the ideal is rarely achieved. The use of persons as free as possible of bias, suggestion, and vested interest is essential. The use as subjects of members of the laboratory staff, physicians, and nurses may lead to erroneous conclusions.

## PEDIATRICS

**Investigations on Immunity After Vaccination Against Diphtheria and Status of Antidiphtherial Vaccination in Amsterdam Children.** A. L. Noordam and A. M. Schrickx. Nederl. tijdschr. geneesk. **101**:141-144 (Jan. 19) 1957 (In Dutch) [Haarlem, Netherlands].

Immunization against diphtheria has been facilitated since diphtheria toxoid has been combined with aluminum phosphate. Investigations carried out on Amsterdam children in 1955 showed that, of the 4-year-old children who entered nursery schools (which are attended by 85% of all children), 57.5% had been immunized against diphtheria; 35.2% had been immunized during the 1st year of life and 22.3% between the 1st and 4th years. Of the 6-year-old children, 95% had been immunized against diphtheria. Of the 4-year-old children who had had their first 2 injections with alum precipitated toxoid about 4 years previously but who had not had a booster injection since then, 92% had a negative Schick reaction, whereas, of those who had not been vaccinated at all, 20% showed a negative Schick reaction, and all those who had received a booster injection had negative Schick reactions. Of the children of primary-school age (6 to 12 years of age), 98% had a negative Schick test. About 25% of the antidiphtherial vaccinations in children under 4 years were carried out by the family physicians and 75% by health officers. In 1955 health officials immunized about 45% of all babies against diphtheria (and whooping cough), and another 10% of the babies were immunized by their family physicians. The authors believe that the propaganda for the immunization of infants against diphtheria should be increased. They also recommend that 2 booster injections should be given, the 1st one when the children are between 4 and 5 and the 2nd when they are between 7 and 8 years of age.

**Clinical and Statistical Correlations in 71 Patients with Tuberculous Meningitis Treated in the Pediatric Clinic of the "Ospedale Maggiore" of Lodi.** F. Brocca and G. Sacchetti. Riv. clin. pediat. **58**:202-212 (Aug.) 1956 (In Italian) [Florence, Italy].

The authors report on 71 children with tuberculous meningitis treated between 1947 and 1956. A 1st group of 12 children was treated with streptomycin combined with a sulfone. Each child received from 21.60 to 43.35 Gm. of streptomycin intramuscularly and from 1.42 to 2.20 Gm. intrathecally. Three of the 6 children who died were in poor condition on admission. Sequelae were not observed, and streptomycin had no toxic effect on the children who recovered. The period of hospitalization for the patients who died was from 4 days to 1 month, and for those who recovered it averaged 5½ months. A 2nd group of 38 children was treated with streptomycin combined with aminosalicylic acid (PAS) and thiosemicarbazone. A total dose of from 15.3 to 64.2 Gm. of streptomycin was injected in each child intramuscularly, and from 0.94 to 4.45 Gm. was given intrathecally. PAS was administered in a dose of from 3 to 6 Gm. per day. Of 20 children who died 10 had come to the hospital in poor condition. The children who recovered were hospitalized for an average period of 5½ months. Relapses occurred in 10 children.

A 3rd group of 21 children was treated with isoniazid combined with streptomycin. Streptomycin was given in a dose of 20 mg. per kilogram of body weight daily for 45 days and then at an interval of 3 or 4 days until a total dose of from 40 to 50 Gm. was reached. Isoniazid was given in a dose of from 10 to 20 mg. per kilogram of body weight until the spinal fluid findings returned to normal and then from 1 to 2 mg. per kilogram of body weight as long as the condition of the patient required. Of 4 children who died, 3 were in poor condition on admission. Four and a half months was the average period of hospitalization for the children in this group who recovered. Superimposed meningitis or relapses did not occur. Sequelae occurred in 2 children. The authors believe that the combination of streptomycin and isoniazid provided the best treatment. Early diagnosis and treatment are necessary for the best results.

**Absorption of Iron from Vegetables in Infants: Value of Homogenized Preparations.** A. Lambrechts, Y. Feuillen and C. Hubin. Rev. méd. Liège **12**:63-65 (Feb. 1) 1957 (In French) [Liège, France].

Twenty-two determinations of iron absorption from the diet were carried out in infants between the ages of 5 and 12 months. They were given milk that was diluted to one-third and to which sucrose and flour was added. They also received soup that was prepared from (1) fresh spinach, boiled and strained (purée), (2) homogenized canned spinach, and (3) fresh spinach, boiled, strained, and treated in a mixer. The iron ingested with the combination of milk and soup

amounted to 1 or 2 mg. daily. The total iron was estimated by the o-phenanthrolin colorimetric method after mineralization. Results showed that the absorption of iron was definitely better when the infants were fed soup made from homogenized canned spinach than when they were fed that made from boiled and strained fresh spinach: The absorption ratio was 12.9% of the ingested amount when fresh spinach treated in the common culinary manner was fed and 32.5% when canned homogenized spinach was fed. The absorption of iron from soup made from homogenized canned spinach was almost identical with that from soup made from fresh boiled spinach treated in a mixer. Homogenized vegetables constitute an alimentary supply that is appealing to the infant. The preparation of vegetables is an important factor that should be considered with regard to iron absorption.

## THERAPEUTICS

**Daptazole and Megimide in Treatment of Acute Barbiturate Intoxications.** K. Madsen. Tidsskr. norske lægefor. 77:60-63 (Jan. 15) 1957 (In Norwegian) [Oslo].

Daptazole and Megimide combined were given to 14 patients in the treatment of barbiturate intoxication. The most notable effect was increased reflex activity and improved respiration, regarded as certain signs of reduction of the depth of intoxication, so that the patients came into a safe state. The patients were closely observed during treatment and awakening. The duration of the coma did not seem to be shortened nor did the barbiturates seem to be eliminated more rapidly. The side-effects were usually moderate. In 1 case paranoid psychosis recurred. The motor unrest was, as a rule, easily controlled. The agents are regarded as valuable in the treatment of deep intoxications, but they are not to be considered as specific barbiturate antidotes and do not in any way make the usual general therapy superfluous.

**Diacetylcolchicine in Antiblastic Therapy.** W. Paolino, G. Pierri and L. Resegotti. Minerva med. 48:1-10 (Jan. 6) 1957 (In Italian) [Turin, Italy].

The authors report the results obtained in 78 patients with different types of neoplasm treated with diacetylcolchicine. The drug given intravenously does not cause local vascular reaction and does not depress the general condition of the patient. Side-effects caused by tropism of the drug on particular tissues were noticed in some patients; mainly, side-effects appeared in patients with forms of neoplasm that were not much benefited from the administration of the drug. Protection of the normal tissues was obtained by giving a small dose of corticotropin intravenously, prednisone by mouth, or ademine intramuscularly. The initial dose of diacetylcolchicine was 7 to 10 mg. This dose was continued, decreased, or given at longer intervals depending on the form of neoplasm and the occurrence of side-effects. The leukocyte count returns to normal after an interruption of treatment for a few days. An initial leukocyte count of 3,000 to 4,000 per cubic millimeter was not considered a contraindication to treatment with this drug. Daily treatment with large doses of the drug was never continued for more than 10 to 15 days, except in patients with chronic granulocytic leukemia. Treatment with a smaller dose (5 mg.) given at intervals of one or more days was never continued for more than 20 to 30 days. Good renal function is a prerequisite for this treatment. Results were excellent and lasting in patients with chronic granulocytic leukemia, excellent but less lasting in patients with reticulosarcoma, good and, in some cases, excellent in patients with malignant lymphogranuloma, good in some patients with lymphosarcoma or pulmonary metastasis due to carcinoma of the breast, and fair in some patients with primitive carcinoma of the lung, in 1 with melanosarcoma, and in 1 with reticuloendotheliosis. The drug had no effect on a patient with fibrosarcoma. Subjective improvement occurred in 2 patients with carcinoma of the ovary. The remission can be maintained by giving a small dose of x-ray and in patients with malignant lymphogranuloma by treating them subsequently with methenamine.

**The Mass Treatment of Tapeworm with Mepacrine.** J. A. McKinnon. East African M. J. 34:15-18 (Jan.) 1957 [Nairobi, Kenya Colony, Africa].

During a routine hygiene inspection in the works camp at Marigat in the Baringo district of Kenya, it was noted that many of the stools contained tapeworm segments. The investigation and treatment of this Taenia infestation provided an opportunity for the trial of the efficacy and safety of quinacrine (mepacrine) in mass treatment. The scheme adopted was designed to provide a measure of laboratory control while the treatment was simplified as would be necessary in mass treatment. The population of the camp was divided into groups of 40 persons, and a timetable was drawn up with 1 day devoted to investigation and treatment of each group and, 3 days later, a day for follow-up investigation of that group. On the treatment day all men in a group were given a dose of 480 grains (31.7 Gm.) of magnesium sulfate on an empty stomach. All stool specimens were examined. Those that did not contain visible tapeworm segments were examined microscopically for tapeworm ova. After that the 494 men (of a total of 1,120 men) whose stools had contained either visible segments (444) or ova (50) were given 0.8 Gm. of quinacrine by mouth in 4 equally divided doses at 5-minute intervals, with sips of an antacid mixture to prevent nausea and vomiting between doses. One hour after the last dose of quinacrine, 960 grains (63.4 Gm.) of magnesium sulfate was given by mouth.

Investigations on the 4th day after treatment showed that 42 of the 494 men still had visible segments in their stools and an additional 70 had tapeworm ova on microscopic examination. This initial failure rate of 22.67% was higher than expected. New tests were made before these men were treated again, and it was found that only 13 had visible segments in their stools and 48 others had tapeworm ova, a total of 61. These patients were re-treated, after which only one man had tapeworm segments and an additional 7 had ova, i. e., 8 out of the original 494 treated.

Three months after the original treatment the 200 men remaining in the camp from the original 494 men treated were examined. Of 170 men who had received only one course of quinacrine, the stools of 4 contained segments and 12 contained ova. Of the 30 men who had received 2 courses of quinacrine the stools of 2 contained ova. The general failure rate in the 200 was 9%. This failure rate and the virtual absence of adverse effects indicate that the use of quinacrine for mass treatment of taeniasis, with suitable adjustment of dosage for children and the chronic sick, is safe and relatively effective and that by this method it should be possible to reduce tapeworm infestation in a community to negligible proportions.

**The Importance of the Intradermal Reaction to Penicillin as an Index of Sensitization.** D. Betetto and M. Graziani. Gior. veneto sc. med. **11:**149-159 (May-June) 1956 (In Italian) [Venice, Italy].

The cutaneous reaction was studied in 150 patients who were being treated with penicillin. The intradermal test was made with a solution containing 1,000 units of crystalline penicillin G per cubic centimeter. An isotonic sodium chloride solution was used as a solvent. The control test was made with an injection of the saline solution alone. Twenty patients (13%) were found to be sensitive to penicillin. An erythematous zone appeared a few minutes after the intradermal injection in 14 patients; the same plus intense itching occurred in 2 patients; erythema and a positive Prausnitz-Kustner reaction occurred in 4 patients. All 20 patients had been previously treated with penicillin; 10 had had a disease considered sensitizing to penicillin; 5 had had bronchial asthma; 3 tonsillitis; 1 trichophytosis; and 1 tuberculous pleurisy. Negative results to the intradermal test occurred in the remaining 130 patients, 68 of whom had never been treated with penicillin. Seventeen of the 130 had in the past been affected with a disease considered sensitizing to penicillin. The authors believe that intradermal tests should be given before subjecting patients to treatment with antibiotics.

**Myleran in Chronic Myeloid Leukemia: Advantage of Systematic Maintenance Treatment.** J. Closon and M. Content. Rev. belge path. et méd. expér. **25:**413-430 (Nov.) 1956 (In French) [Brussels].

Six patients with chronic myeloid leukemia were treated with busulfan (Myleran). Therapy consisted in giving large initial doses (2 to 8 mg. daily) for 10 to 22 weeks and maintenance doses of 2 to 6 mg. per week for 12 to 16 months. The whole treatment was extended over a period from 14 to 21 months with a total dosis of 660 to 950 mg. of busulfan. Excellent remissions up to 2 years were obtained in 3 pa nts. The antimitotic agent was well tolerated by 5 patients. Untoward reactions due to idiosyncrasy and to an acute fatal evolutive phase of the disease occurred in one. The chief advantage of busulfan is its efficacy when radiotherapy has been of limited or no value. Maintenance therapy requires monthly blood cell counts. The advantage of prolonged treatment with busulfan is limited by a progressive resistance of the leukemic cells to the drug. In this case, combined treatment with busulfan and x-rays should be given. The treatment with busulfan seems to be more effective than x-ray therapy. It is, therefore, the treatment of choice in chronic granulocytic leukemia.

## PATHOLOGY

**Investigation of Non-Ulcer Dyspepsia by Gastric Biopsy.** A. W. Williams, F. Edwards, T. H. C. Lewis and N. F. Coghill. Brit. M. J. **1:**372-377 (Feb. 16) 1957 [London].

The authors consider dyspepsia a condition in which abdominal or thoracic symptoms other than dysphagia occur in relation to eating. Nonulcer dyspepsia implies the occurrence of such symptoms when no ulcer can be found in the esophagus, stomach, or duodenum not previously operated on. A group of 775 patients with dyspepsia was studied by means of a barium-meal. The examination was repeated and gastroscopy was performed when there was doubt about the results. Of this group, 459 (59.2%) were men and 316 (40.8%) women. Investigation revealed a likely organic cause for the dyspepsia in 307 (39.6%): duodenal ulcer in 195, gastric ulcer in 79, gastric and duodenal ulcers in 7, hiatal hernia in 16, esophageal reflux in 3, gastric carcinoma in 3, cardiospasm in 2, esophageal ulcer in 1, and volvulus of the stomach with eventration of the left side of the diaphragm in 1. Investigating gastritis as a cause of dyspepsia, biopsies of the gastric mucosa were obtained in 200 patients with nonulcer dyspepsia. The authors consider several categories of mucosal lesions, and an analysis of the results when multiple specimens were obtained showed agreement between them in 80 to 90% of the cases. There was evidence that the greater the number of samples examined the greater the chance of finding atrophic gastritis. The mucosa was normal in 45% of these 200 patients. There were mild changes—mainly those of chronic gastritis—in 36% (miscellaneous group) and more severe in 4.5% (superficial gastritis). A diagnosis of chronic atrophic gastritis was made in 14.5% of the patients. There were no notable differences in the incidence of gastritis between the sexes, but the atrophic type became more frequent as age advanced. The milder changes occurred about as frequently at all ages. Hydrochloric acid production on histamine stimulation fell away as severity of gastritis increased.

**Attempt at Anatomopathological Classification of Chronic Pancreatitis: Comparison with the Pancreatographic Aspects.** H. Leger and L. Leger. Presse méd. **64:**2168-2172 (Dec. 25) 1956 (In French) [Paris].

Many difficulties are encountered in attempting to define the pathological processes responsible for the lesions found in biopsy specimens obtained from patients with chronic pancreatitis. Careful study, however, has shown that, in spite of the varied and often complex changes evident in the slides, a search for the dominant histopathological element will supply information suggesting the cause of the condition and indicating the methods that should be used in at-

tempting to correct it. Thus the predominance of ductal dilatation accompanied by gross sclerosis, but with little derangement of the lobules and few changes in the acini, suggests obstruction of the excretory passages and indicates a need for a procedure providing drainage or retrograde decompression. Again, the special picture presented by paraneoplastic pancreatitis, with or without ductal dilatation, should lead to a search for the tumor and to wide excision. Finally, the topographic distribution of the sclerosis that develops in the course of portal hypertension, chronic endarteritis, and various other conditions produces pictures that are distinctive enough to be easily recognizable, but, even in these cases, such factors as the primary acinic changes, the phenomena of duodenal congestion, spasm of the sphincter of Oddi, and abrupt changes of pressure in the ducts may favor ductal disturbances and distention from above that are also perfectly apparent in the histological specimens and that may be susceptible of improvement by a drainage or bypassing procedure.

A distinctive picture generally recognizable in biopsy specimens taken from peripheral zones, but not including the important excretory ducts close to the pancreatic duct, can be drawn up for each of the principal types of chronic pancreatitis. Paraneoplastic pancreatitis, for instance, is accompanied by many changes, but those that seem to be the most characteristic are the special distribution of the fibrosis that develops between the acini, forcing them more or less widely apart, and the increase in the volume of the acini with cellular hyperplasia or else their tendency to atrophy and destruction. These changes are apparently linked as much to the so-called desmoplastic properties of the neighboring tumor as to the inflammatory and degenerative phenomena produced by the rupture of the acini, which undergo progressive distention while retaining a certain secretory activity. Pancreatography in patients with cancer reflects quite faithfully the dilatation of the principal duct, which is always pronounced, while little change is seen in the smaller ducts—facts that have been noted histologically by others.

The term ductal pancreatitis with fibrosis and ectasia is reserved by the authors for the changes produced, principally in the excretory passages, as a result of distention, stasis, or obstruction of any kind other than cancerous. The condition referred to as pancreatitis due to obstruction, in which an obstruction to the outflow of pancreatic juice is recognized, sometimes exists in the pure state, but it may also be associated with pancreatitis of a different type, either primary or accompanying hepatic cirrhosis. Relapsing pancreatitis is characterized by clearly enlarged interlobular spaces, sometimes presenting a fairly compact fibrous appearance and sometimes loose and edematous with many dilated and congested vessels. Dilatation of the excretory ducts and a certain amount of peripheral fibrosis are also found in many cases, but these changes are always subordinate to those produced by vasomotor disturbances. Finally, the earliest changes in primary fibrous pancreatitis are those affecting the differentiated acinic cells. The fibrosis, which appears as a reparative process only after cellular degeneration, develops at the periphery of the lobules in contact with the cells that are most affected. Examples of these changes may be found in pancreatitis accompanying alcoholic cirrhosis of the liver, pigmentary cirrhosis, and anemic syndromes, and in chronic fibrous pancreatitis of arterial origin.

**So-Called Xanthomatous Biliary Cirrhosis and Chronic Pseudoxanthomatous Pericholangitis.** G. Hartmann. Frankfurt. Ztschr. Path. **68**:55-63 (No. 1) 1957 (In German) [Munich, Germany].

Xanthomatous biliary cirrhosis is characterized by (1) mechanical (obstructive) jaundice that persists for years, fluctuates only slightly in intensity, and is accompanied and often preceded by pruritus; (2) hepatosplenomegaly with induration, in which the liver surface is at first smooth and later hob-nailed and in which ascites appears either late or not at all; (3) cutaneous xanthomas on the face (particularly the lids), the upper extremities (especially elbows and fingers), the distal parts of the lower extremities, and occasionally also in the axillary and gluteal folds; and (4) severe hyperlipoidemia, in which the cholesterol value is from 4 to 10 times higher and the lecithin value from 4 to 8 times higher than the normal. The serum remains transparent because of the rather low neutral-fat content. The disease usually ends in death from hepatic insufficiency or from hemorrhage from ruptured esophageal varices. It occurs chiefly in women. The pathological changes in the liver were thoroughly investigated by MacMahon who characterized the lesion as a pericholangiolitic biliary cirrhosis.

The author describes the history of a 50-year-old woman who had had pruritus for several years and who was hospitalized because of the recent development of jaundice. Her urine had become dark brown, and the stools were very light. Her liver and spleen were enlarged and indurated. Because the jaundice suggested obstruction an exploratory laparotomy was performed. This revealed a normal gallbladder and no obstruction in the extrahepatic bile ducts. Conservative therapy produced no improvement. Later the patient had an attack of herpes zoster and hemorrhoids. Because the jaundice continued, the patient was again subjected to laparotomy, but the gallbladder and large bile ducts again proved normal. A wide cholecystogastrostomy was made. A biopsy specimen was taken from the edge of the liver. Studies revealed that the pathological substrate of the chronic jaundice was a granulomatous cholangiolitic or pericholangiolitic and partially xanthomatous liver disease. Since the bile retention was caused by obstruction of the smallest intrahepatic bile ducts, it is understandable that the cholecystogastrostomy was ineffective and that jaundice persisted. Later symptoms appeared that indicated hemorrhagic diathesis.

The exact cause of xanthomatous biliary cirrhosis is unknown, but the inflammatory blockage of the junction between the intra-acinary bile capillaries and the interlobular bile ducts may be the key point. The granulomatous process there becomes complicated by the simultaneous disturbance in the lipoid metabolism. The author does not believe, however, that the

disturbance in the lipoid metabolism is the initial factor. The histological changes in the liver seem to represent an atypical, cholangiolitic biliary cirrhosis, and, only exceptionally, may the process be characterized by transient honeycomb structures in the cholangiolitic granulation tissue. The changes in the tissues might then resemble those in lipoid nephrosis: First the epithelia of the junction ducts and of the terminal bile ducts become loaded with the flood of lipoids and finally degenerate, and adjacent histiocytes absorb the liberated cholesterols so that epithelial and mesenchymal honeycomb cells appear. Excessive production and retention of lipoids produce the hyperlipoidemia, and this, in turn, causes the deposition of the adventitial histiocytes in various locations, particularly in the skin. The fact that the cholesterol metabolism in women is unstable because of endocrine factors, particularly during the menopause, may explain the predisposition of women to xanthomatous biliary cirrhosis. As a counterpart to this disease, in which an unknown pathogenetic factor seems to act chiefly in the smallest intrahepatic biliary passages, the author describes the case of a 74-year-old woman who had had recurrent attacks of jaundice since the age of 18. In this patient extraordinary proliferations of honeycomb cells were found in the larger interlobular bile ducts. The changes in this patient were due to an entirely different process. Here there existed chronic, sometimes suppurating intrahepatic cholangitis with pseudoxanthomatous pericholangitis.

**Alcaligenes Faecalis and Human Pathology: A Study of 80 Strains.** E. Enjalbert, L. Lapchine and Tran-Van-Tho. Toulouse méd. **58**:45-60 (Jan.) 1957 (In French) [Toulouse, France].

Contrary to the general assumption that Alcaligenes faecalis is a normal saprophytic inhabitant of the intestinal tract in man and animals, the authors emphasize that it is an abnormal inhabitant of the intestines in man and that it is associated with various infections. Eighty strains of this organism were isolated from the blood, spinal fluid, endobronchial biopsy specimens, pleural fluid, urine, throat smears, and feces of patients with sore throat, meningitis, bronchitis, tuberculosis, cancer of the lung, suppurative conditions, and gastroenteritis. The sensitivity of 65 of the 80 strains to antibiotics was tested; 13 strains were resistant to all the common antibiotics; 4 were sensitive to penicillin, 36 to chlortetracycline, 39 to chloramphenicol, 47 to oxytetracycline, and 23 to streptomycin. Clinically, chloramphenicol had the most rapid effect. A. faecalis has been erroneously considered by other workers as a "contamination" of the examined specimens. It is the only one of the Achromobacteriaceae associated with acute generalized infections of the typhoid type and with various localized infections in man. Spontaneous recovery occurs frequently, and one should refrain from treating the infection too rapidly and too vigorously. Even recovery from the acute meningitis occurs more easily than from meningitis caused by other gram-negative bacteria. Localized infections require treatment with an effective antibiotic, but the causative agent is rapidly destroyed when it is reached by the drug. The risk of the appearance of more and more dangerous resistant strains after prolonged treatment with antibiotics is less of a threat with A. faecalis than with other bacteria such as Proteus and Pseudomonas, and it does not seem that the part played by the antibiotics is a very disturbing one.

**Dangerous Irregular Blood Type Antibodies: Report on Danish Material Comprising 450,000 Blood Specimens.** J. Andersen and G. Munk-Andersen. Ugesk. læger **119**:31-37 (Jan. 10) 1957 (In Danish) [Copenhagen].

Examination of 450,000 blood specimens, 125,000 of them from pregnant women, for the occurrence of dangerous irregular-blood-type antibodies revealed anti-Rh, antibodies to D, CD, and DE, in 2,007 persons and antibodies to C, E, c, e, f, K, S, $Fy^a$, and $Jk^a$ in 100 persons. On the basis of the frequency of immunization recipients for blood transfusion are divided into 3 categories, (1) especially exposed recipients—persons previously given transfusion and women who have given birth to children with signs of hemolytic disease or whose history is suspect in this regard, (2) less exposed recipients—women who have been or are pregnant but have not born children with signs of hemolytic disease, and (3) ordinary recipients. In group 1 the frequency of all immune antibodies is especially high, and these patients should therefore be given transfusion only after an extended compatibility test. In group 2, although an extended compatibility test is not so necessary, it should be made. In group 3 the classic compatibility test in object glass suffices. The practical value of the group classification of recipients depends on how carefully the history of transfusion and pregnancy is taken. Persons in whom an irregular immune antibody has previously been established, including anti-Rh, constitute a special group in which blood transfusion should be given only after an extended compatibility test even though it is a matter of donors found to be negative with regard to the blood type characteristic involved.

## RADIOLOGY

**Bone Lesions in Patients with Irradiation Ulcers.** J. Kolár and R. Vrabec. Strahlentherapie **102**:112-125 (No. 1) 1957 (In German) [Munich, Germany].

In 34 patients with irradiation ulcers the authors studied the condition of the bones underneath these ulcers. In 24 the irradiation had been given for tumors. In 5 the irradiation ulcers appeared 3 months after the last irradiation whereas in the others the interval between irradiation and ulceration ranged from 1 to 15 years, averaging about 6½ years. In 11 of the patients the bone lesions involved the thorax (ribs or sternum), in 9 the pelvis (mostly the neck of the femur), in 6 the extremities, in 5 the vertebral column, and in 3 the

skull. Roentgenologic examination does not reveal the serious histological changes, furthermore, as with the skin lesions, the irradiation damage in the bone may progress for years. Neither the onset nor the ultimate prognosis of the bone lesion can be ascertained. The authors observed the following bone lesions: osteoporosis, structural transformation of the substantia spongiosa and corticalis, well-defined or indistinct areas of decreased density, Sudeck's bone atrophy, spontaneous fractures, and necrosis and destruction of bone and cartilage.

Factors that differentiate bone lesions produced by irradiation from those resulting from metastasis included: localization in the irradiated region and the absence of similar lesions in other bones; slow progression and sometimes a tendency to cure, not taking place spontaneously in metastases; benign nature of the lesion as proved by the fact that of 24 patients in whom tumors were irradiated 18 have so far survived more than 5 years; and the fact that renewed irradiation increases the bone lesion. Biopsy furnishes further proof, but the authors avoid it because of the risk of infection in the necrotic bone. Conservative treatment was used in 5 patients but proved ineffective in 2. In 29 patients plastic repair was carried out, and in 6 of these necrotic bone had to be removed. Necrosis in transplanted tissues and wound infections demonstrated that the vitality of the tissue was greatly reduced.

**Clinical Aspects and Therapy of Melanomas.** G. Miescher. Strahlentherapie **102**:1-20 (No. 1) 1957 (In German) [Munich, Germany].

Miescher designates the malignant form of the proliferation of melanoblasts as melanomalignoma, pointing out that this term should replace the terms melanocarcinoma and melanosarcoma. In the development of melanomalignomas the precancerous, circumscribed melanomas are important. They generally appear as pigmented spots that are characterized by extreme irregularity of contour and pigmentation. They may contain not only brown but also gray-brown and blue-black pigments. These pigmented spots may appear also on the mucosa. Melanomalignomas may develop from them after many years. The decision of whether malignancy exists may prove difficult, but it is inadvisable to attempt clarification of the diagnosis with biopsy, because this involves the danger of metastasis.

Opinions are still divided about the treatment of the melanomalignomas, some regarding resection and others irradiation as the treatment of choice. In the author's series of 98 patients, 74 were still free from metastases when last seen. These patients were treated during different periods, and in some the primary treatment was resection and in others irradiation. The results obtained indicate that the presence of metastases at the time of treatment is the most important factor in the prognosis. Melanomalignomas are curable in a high percentage of cases, provided treatment is started before the development of metastases. Neither the surgical nor the radiologic method is necessarily superior, provided either method is carried out appropriately. In the treatment of difficult cases, surgeons and radiologists should collaborate. Although the treatment of the melanomalignomas is difficult, this is not the case in the precancerous melanotic stage. In 37 patients with such lesions the author achieved ideal results with grenz ray therapy.

## ANESTHESIA

**A New Technique of Treatment For Intractable Pain: Prefrontal Infiltration with Procaine by Supraorbital Route.** J. Sigwald, D. Bouttier, C. Piot and others. Semaine hôp. Paris **33**:400-402 (Jan. 30) 1957 (In French) [Paris].

The authors used a new technique for the relief of intractable pain in patients with cancer. After local anesthesia of the roof of the orbit with a few cubic centimeters of procaine, a trocar containing a pointed stylet was inserted through the upper eyelid at a distance of about 1 cm. from the outer canthus and about 5 mm. below the orbital arch. After the indented point of the trocar had come into contact with the bone, the stylet was pulled back, and a stainless steel bit, firmly fixed to a holder, was introduced into the lumen of the trocar in such a manner that its length did not exceed that of the trocar by more than 2 or 3 mm. Thus any risk of severely damaging the substance of the brain was prevented, and the plate of the frontal bone was pierced easily, with the aid of a slightly rotatory movement. The bit, then, was pulled back and replaced by a long needle with a blunt end, containing a stylet. This trocar was then inserted into the frontal lobe. The needle was pulled back and aspiration was performed with the aid of a syringe to make sure that the cerebral ventricles had not been affected. In the absence of any ventricular fluid, 10 cc. of procaine hydrochloride was injected slowly. The entire procedure required 10 minutes and was repeated immediately on the other side.

Twenty infiltrations were performed according to this technique with excellent results in 7, satisfactory results in 10, and failures in 3. Among the excellent results was that obtained in a woman with cachexia and cancer of the stomach who had obtained only little relief of pain from 3 daily injections of morphine and who became euphoric after her first infiltration with procaine hydrochloride. Pain was completely relieved for 12 months. A mild recurrence was controlled with another infiltration, and she survived for a year without suffering. Other patients were greatly improved so that morphine injections were required less frequently or morphine treatment could be discontinued completely. In most patients, improvement, however, was only temporary and another infiltration became necessary after from 8 to 15 days. It was repeated 3 or 4 times before complete failure became apparent. Neither mental disturbances or disturbances of character occurred in any of the patients. Syncope occurred in 1 patient and apparently was caused by

the passage of a few drops of procaine hydrochloride into one of the lateral ventricles. Mild headache for several days was observed in a few patients. A severe cerebral hemorrhage occurred in 1 patient with cancer of the stomach who was in poor condition on admission. The prefrontal infiltration was done with the aid of general anesthesia and displacement of the trocar in the frontal lobe resulted from an inopportune movement. The patient became semicomatose after the infiltration and died the next day. Autopsy revealed a hematoma the size of a nut in the injected prefrontal lobe.

## PHYSIOLOGY

**Physiology and Toxicology of Tritium in Man.** E. A. Pinson and W. H. Langham. J. Appl. Physiol. **10**:108-126 (Jan.) 1957 [Washington, D. C.].

Tritium was used as a tracer for hydrogen of mass one (protium) in biological experiments. The advantage of tritium over deuterium is that it is radioactive. The rate of entry of tritium into the body as water (HTO) and as gaseous hydrogen through the principal routes, the rate and extent of distribution and fixation of tritium in tissues in various parts of the body, and the rate of tritium excretion were studied on the basis of 5 experiments on 3 normal men, for the evaluation of the health hazards to personnel exposed to tritium either chronically or acutely in laboratories or industrial plants. HTO absorption through the gastrointestinal tract was complete in 40 to 45 minutes. The volume of water transferred from the intestine to the blood was linear with time and proportional to the volume of water ingested within the range of 100 to 1,000 ml. When exposed to HTO vapor by inhalation, man absorbed 98 to 99% of the radioactivity inspired.

The activity in venous blood increased steeply during and shortly after exposure to the inhalation of tritium. Then it declined exponentially to equilibrium with a half time of about 12 minutes. The average dilution volume was 62.2%. The biological half time of tritium in the body fluid of 8 men on ad libitum water intake averaged 11.5 days. HTO was absorbed by man through the skin at a rate comparable to that of insensible perspiration at equal vapor pressures. The HTO entering the body through the total skin was about equal to that entering the lungs. Man slowly oxidized inspired protium-tritium molecules to HTO. The radiation hazard from exchange of tritium with hydrogen of the tissues after exposure to HTO was insignificant compared to the hazard from the amount of HTO necessary to induce appreciable radioactivity in the tissues. The maximum permissible concentrations of tritium oxide in air and water was estimated at $5 \times 10^{-6}$ $\mu$c per milliliter and 0.1 $\mu$c per milliliter respectively for continuous 24-hour exposure. Adoption of the recommendations of the International Commission on Radiological Protection will result in the division of these values by 3 and the maximum permissible body burden of tritium will become about 1.2 mc.

**The Effect of Adrenaline Infusion on Human Blood Coagulation.** G. D. Forwell and G. I. C. Ingram. J. Physiol. **135**:371-383 (Feb. 15) 1957 [Cambridge, England].

Experiments performed by Cannon and co-workers in anesthetized animals in 1914 revealed a shortening of the clotting time after the administration of epinephrine. The main experiments of these workers were repeated by the authors in anesthetized cats and dogs. By using Cannon's technique, his observations were confirmed, but the results obtained with this technique could not be reproduced with standard methods. It remains, therefore, uncertain what function of clotting Cannon may have measured. Of 22 male volunteers in whom clotting times in silicone-coated tubes and direct eosinophil counts were obtained by serial venipuncture at half-hour intervals, 8 drank a solution of 50 Gm. of fructose after the 1st venipuncture and 14 received instead 50 Gm. of destrose. Blood dextrose and fructose concentrations were also determined. A correlation between the clotting time and the eosinophil count was observed in these men. This suggested that the effect of repeated venipuncture was an important variable in experiments comparing the clotting of consecutive blood samples and that the effect might be assessed by the behavior of the eosinophil count.

Twelve control infusions and 13 epinephrine infusions then were given to 9 healthy young medical students who were well-habituated to venipuncture. The difference in clotting time between blood samples obtained from venipuncture before and after the infusions of epinephrine was compared with the difference in clotting time between blood samples obtained from consecutive venipunctures spaced at about the same intervals during the control infusions. Only after the epinephrine infusion was a significant fall in clotting time demonstrable in the silicone-coated tubes. This was not seen in the glass tubes. This finding suggested that the fall in clotting time was a real effect of the epinephrine and that the effect of the drug was mediated through the initial stages of clotting not later than the development of intrinsic thromboplastin. More detailed studies of the clotting mechanism were made after 7 of the epinephrine infusions, and the results suggested an increase in the activity of clotting factor 5.

**Observations on a Case of External Pancreatic Fistula in Man.** I. S. R. Sinclair. Brit. J. Surg. **44**:250-262 (Nov.) 1957 [Bristol, England].

Physiological responses of the pancreas were studied in a 47-year-old man in whom a pancreatic fistula developed after subtotal gastrectomy for duodenal ulcer. The daily output of pancreatic juice seems to be greater than has often been taught; 1,500 ml. is not considered indicative of pathology. The rate of pancreatic secretion fell to levels lower than those previously recorded in man. This slight secretion is considered to be mainly the result of continuing stimulation by the vagus. The sodium concentration in the pancreatic juice is higher than that in the

serum. The low estimates of calcium concentration in the pancreatic juice given by some previous workers may be explained on the basis of a technical error in the method of estimation. The reciprocal relationships between chloride and bicarbonate concentration were confirmed and some evidence is presented that a similar relationship exists between sodium and potassium ions.

Attention is drawn to the dissociation between the volumetric and bicarbonate responses after stimulation of the pancreas. In general the responses to various drugs confirmed previous reports, but the effect of prostigmine was variable and in tests of pancreatic function this drug should not be used to stimulate secretion. Various pure foodstuffs were tested as stimulants of pancreatic secretion. Carbohydrate proved a much more powerful stimulant than either protein or fat. Administration of carbohydrate directly into the jejunum resulted in a brisk flow of pancreatic juice. Intravenous infusions of carbohydrate or protein hydrolysates did not stimulate pancreatic secretion. The absence of a psychic phase of pancreatic secretion in man was confirmed, as was the failure of the broad-spectrum antibiotics to reach the pancreatic juice.

**Divergent Results in Sex Determination on the Nuclei of Leukocytes and of Oral Epithelial Cells.** W. Kosenow. Klin. Wchnschr. 35:75-76 (Jan. 15) 1957 (In German) [Berlin].

Kosenow points out that, whereas at first skin biopsy was resorted to for the determination of the sex chromatin, it is now customary to search for the differentiating sex chromatin in the nuclei of leukocytes and of oral epithelial cells (obtained by means of a spatula from the buccal mucosa). These latter methods are preferred because they obviate the need for biopsy. On the other hand these methods represent an additional means of verification. In all tests on healthy children the diagnosis "chromosomal male" and "chromosomal female" corresponded with the true sex. Of 15 phenotypically female patients with gonadal dysgenesia, 11 proved to be genetic males and 3 genetic females on the basis of the sex chromatin in the nuclei of the oral epithelial cells as well as of the leukocytes in blood smears.

The one exception was an 18½-year-old girl of low stature (32 cm. [12½ in.] below normal) with hypogenitalism and skeletal changes in the form of osteoporosis, scoliosis, and retarded development of the centers of ossification of the bones of the wrist. No ovaries were found at laparotomy. In this patient blood specimens (nuclei of leukocytes) were repeatedly examined for the sex chromatin (always by 2 examiners). The quantitative occurrence of the mass of chromatin indicated that this patient was a chromosomal male. The results of the search for the sex chromatin in the nuclei of the oral epithelial cells, however, gave a decidedly different result. Three investigators examined specimens from the oral mucosa of this patient, counting 200 cells, and found 22, 16, and 25 with chromatin-positive (female) nuclei. While these figures are below the averages obtained by other investigators, the authors believe that they indicate a "chromosomal female." About 10% of the chromatin-positive cellular nuclei had not only 1 but 2 chromatin bodies. The search for the double sex chromatin was made by 2 investigators both of whom found that 9 or 10 of 100 cells whose nuclei contained the sex chromatin had 2 masses of female sex chromatin. The divergent results of the 2 methods in this patient cannot be explained by the authors. They believe that this observation demonstrates the importance of always making several tests before making a diagnosis of the chromosomal sex in patients with gonadal dysgenesia. They also suggest that studies be made on a larger number of such patients to ascertain whether the observed divergence of test results is due to technical defects or whether different combinations of sex chromosomes or anomalies of the accessory chromosome exist, which might throw more light on such abnormalities.

**Individual Variations in Expenditure of Energy.** J. Booyens and R. A. McCance. Lancet 1:225-229 (Feb. 2) 1957 [London].

It has generally been accepted that variations in individual caloric intakes are due to differences in age, size, and muscular activity at work and recreation, tempered to some extent by the degree of efficiency and training of the subject. It has also been shown that in any homogeneous group of adults or children, there are always some who have caloric intakes greatly in excess of those of others and that the differences cannot necessarily be explained by size or observed muscular activity. The results of investigations had indicated that differences in the energy expended during lying and sitting might be responsible for large individual variations in caloric intake, and it was suggested that similar differences might underlie the facility with which some people appear to put on weight, whereas others do not. The authors checked the findings of other investigators and studied the caloric expenditures of some people who utilize large or small amounts of energy when they are lying, sitting, and standing. Their studies were made on 14 women and 22 men, ranging in age from 20 to 57 years. Apart from a few science students, all the subjects were attached to the Department of Experimental Medicine and were accustomed to the idea of experimental work; hence psychological influences were largely eliminated. The metabolic rates were determined while the subjects were (1) in the basal state, (2) sitting on a comfortable upright chair, and (3) standing. Three had rates more than 30% below and 1 a rate of more than 24% above the average for the group for all 3 occupations.

The energy balance sheets of these 4 and of 2 other persons were investigated for 7 or 14 days. The intake was measured by weighing the food and the output by a time-and-motion study, combined with measurements at the important occupations. It was concluded that (1) the limits usually accepted for the normal basal rates are too narrow and (2) an unusual rate for

lying, sitting, and standing may make a great difference to the total daily expenditure of energy, but (3) although a small expenditure at these 3 occupations may lead to a small energy requirement, it does not necessarily lead to obesity or even to a tendency to put on weight. It was thought at the outset of this study that if persons were found with exceptionally low metabolic rates lying, sitting, and standing they might all tend to be fat and have trouble in keeping their weight within normal bounds. Two subjects were found to have this trouble, but 2 others were both exceptionally thin and did not have to worry about the food they ate in spite of their low metabolic rates. One man who had a high metabolic rate while lying, sitting, and standing was large and maintained his weight easily. Another subject was a woman of normal proportions. These masked variations in expenditures of energy explain well enough why some people require few calories to maintain their weight and others twice as many, but there is nothing to suggest that they play any part in the fundamental control of appetite. This problem remains to be solved. The food served in the society in which we live and the food eaten by habit and convention are adjusted unconsciously to suit the person who is average in all respects. Persons with low expenditures of energy, whether obvious or masked, can only maintain or retain an average weight if they stop eating the strictly conventional amounts of food.

## PUBLIC HEALTH

**Study of Antipoliomyelitis Antibodies in Children and Young Adults in the Canton of Vaud.** B. Baudrez, V. Bonifas, C. Piguet and C. Wild. Schweiz. med. Wchnschr. 87:77-81 (Jan. 26) 1957 (In French) [Basel, Switzerland].

In the spring of 1955, the health authorities of the canton of Vaud undertook a preliminary immunological investigation designed to facilitate the choice of candidates for antipoliomyelitis vaccination. The presence or absence of the 3 types of antipoliomyelitis antibodies was investigated in (1) school children, aged 7 or 8; (2) school children, aged 11 or 12; and (3) normal-school students, aged 18 or 19. Groups 1 and 2 were subdivided into rural and urban subgroups. The percentage of children in the 7-to-8-year age group with antibodies of at least 1 type was significantly higher among the rural than it was among the urban children, 76% as compared with 61%. A significant difference was also found between the town and the country children in regard to the number of those in the 7-to-8-year age group with both type 1 and type 3 antibodies. In the 11-to-12-year age group, the difference was no longer significant.

Infection with 1 type of poliomyelitis virus is known to produce specific antibodies capable of neutralizing, in vitro, only that particular type of virus. The findings in clinical cases, however, suggest that there is a certain degree of cross protection so that an earlier infection with a type 2 virus provides some protection against the paralysis caused by a type 1 infection. The percentages of persons immunized against all 3 types of virus in this study were 4.2% for children aged 7 or 8, 14% for children aged 11 or 12, and 6% for young adults aged 18 or 19. Analysis of the distribution of antibodies in relation to age showed that in the 11-to-12-year and 18-to-19-year age groups, 1 in every 5 inhabitants of the canton possessed no antipoliomyelitis antibodies and so ran the risk of contracting poliomyelitis in case of exposure to the virus. Since the relation between clinically manifest poliomyelitis and inapparent cases in persons exposed for the first time to the virus increases with age, it follows that the danger of contracting paralytic poliomyelitis increases between the ages of 12 and 18. The serologic findings in this series support the endemoepidemiologic observations in the canton in recent years, in which almost as many cases of paralytic poliomyelitis have been found in adults as in children.

The study of serologic immunity shows that a certain number of the persons in a population are not protected against poliomyelitis. A population normally lives in a state of equilibrium in relation to the poliomyelitis viruses, with only a small proportion of the nonimmune persons contracting the disease. The equilibrium, however, may be disturbed so that from time to time the incidence of the disease rises, although the distribution of cases by age groups remains unchanged. Antipoliomyelitis vaccination is indicated as a matter of principle because the conditions that may lead to an increase in the incidence of the disease are not subject to control, and the findings in this study suggest that young children, because they are the most susceptible to infection, should be the first to be vaccinated.

**Ethnic Differences in the Incidence of Leukemia.** B. MacMahon and E. K. Koller. Blood 12:1-10 (Jan.) 1957 [New York].

That leukemia is recorded as cause of death less frequently among American Negroes than among white persons has been well authenticated. The authors made an attempt to estimate the incidence of leukemia in relation to religion and country of birth, using data collected from clinical records and death certificates in Brooklyn. A series of 1,636 white patients in whom leukemia was diagnosed in the period 1943-1952 is compared with selected census data for the population. The incidence of leukemia in the native population of Brooklyn was 45.3 and in the foreign-born population 61.0 per million per annum. The large proportion of Russian-born persons in the population seems to account for the higher rate in the foreign-born group. Catholic and Protestant groups did not show any difference in susceptibility to this disease. United States vital statistics show that the commonly observed difference in leukemia death rates between white persons and Negroes is associated with social differences between the 2 groups. Little or no difference in leukemia death rate was seen between these 2 groups in Brooklyn.

# BOOK REVIEWS

**Wire Brush Surgery in the Treatment of Certain Cosmetic Defects and Diseases of the Skin.** By James W. Burk Jr., M.S., M.D., Associate Professor of Clinical Medicine (Dermatology), Tulane University of Louisiana, School of Medicine, New Orleans. Publication number 300, American Lecture Series, monograph in Bannerstone Division of American Lectures in Dermatology. Edited by Arthur C. Curtis, M.D., Chairman, Department of Dermatology and Syphilology, University of Michigan Medical School, Ann Arbor. Cloth. $6.75. Pp. 154, with 68 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1956.

This monograph presents an inclusive, well-illustrated, and readable summary of the current status of dermabrasion for scarring and other skin changes, with particular reference to scarring following acne. The author has summarized the literature on the subject adequately, and has written his book from a background of personal experience. There is a digest of the anatomic and histopathological principles that bear on the procedure and a detailed outline of the equipment and supplies required, the comparative virtues of ethyl chloride and Freon 114 for producing freezing and local anesthesia, the techniques of the method, postoperative management, complications, indications, and contraindications.

The essential procedures and instruments for carrying out dermabrasion were described in several publications by Kromayer in Germany, in 1905. Curiously enough, his methods appear to have received little or no trial in the United States until the reintroduction of the sand-papering technique in the mid-1940's. This technique had a number of disadvantages, one of the most serious of which was the formation of silica granulomas in the abraded area. The late Dr. Abner Kurtin of New York repopularized and refined the method of dermabrasion, and must be credited with the development of the technique as it is used today by dermatologists and plastic surgeons. From its original restriction to the treatment of scars from acne, chickenpox, or trauma, and attempts at removal of tattoo marks, the method has been widely extended to include treatment of various benign epidermal tumors, rhinophyma, and many of the excrescences and other morphologic changes of aging.

On the basis of thousands of cases of acne scarring treated by this method since 1953, there can be no doubt that significant cosmetic improvement can be obtained in well-selected cases, and that the risks are relatively small in the hands of competent operators. The human skin, fortunately, is endowed with extraordinary self-reparative powers. Because the epidermal pegs extend deeply into the skin in most areas, the epidermis is capable of regrowing after vigorous abrasion, even to the point of exposure of small islands of subcutaneous tissue. If it is then let alone, and does not become infected or undergo hypertrophic scarring, the surface of the regenerated skin looks better than it did before.

The author is well aware of dangers of overenthusiasm in any surgical procedure undertaken to remedy a cosmetic defect. However, the risks of the method are so small and the improvement so definite as to justify its use in patients who have significant scarring following acne or some other inflammatory process. There can also be little objection to the use of the method in obviously benign epidermal tumors such as seborrheic keratoses. In the case of tattoo marks, in which the pigment is subepidermal, the method is far less successful. Its use in improving the wrinkling of age and in removing freckles and other melanin pigmentary deposits should be approached with great caution. In the case of pigmented nevi, the author states that, "with the exception of obviously benign non-pigmented nevi, a punch biopsy should precede planing." The only difficulty with this concept is that the gross criteria for recognition of nevi of junction type, either inactive or active, are still not as clearly defined as they might be. It is reassuring that no undetected melanomas have been reported after the use of this method, but certainly it cannot be regarded as an acceptable method of removal of pigmented nevi. As a commentary on the bacteria-laden environment of hospitals, the author reports that the two instances of postoperative infection he encountered occurred in hospitalized patients. He regards outpatient treatment as preferable. This is a balanced and informative book.

**Chronic Illness in the United States. Volume II: Care of the Long-Term Patient.** By Commission on Chronic Illness. Cloth. $8.50. Pp. 606, with illustrations. Published for Commonwealth Fund by Harvard University Press, Cambridge 38, Mass.; Oxford University Press, Amen House, Warwick Sq., London, E.C.4, England, 1956.

This is the second volume in a series of four reports by the Commission on Chronic Illness. The Commission is sponsored by the American Hospital Association, the American Medical Association, the American Public Health Association, and the American Public Welfare Association. Thirty-nine other national organizations in the health field participated in the 1954 conference, the conclusions of which are the basis for the observations and recommendations appearing in this volume. The book's eight chapters deal with the long-term patient, the patient at home, rehabilitation at home and in institutions, the patient in an institution, personnel and education, coordination and integration, research for planning and administration, and financing. Seven appendixes deal with special phases of the general subject.

The "long-term patient" needs definition. Not all who are afflicted with chronic disease need constant or regular medical care. As defined by the Commission, a long-term patient is one suffering from chronic

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

disease or impairment, who requires a long period of care for a continuous period of at least 30 days in hospital or three months in an institution or at home and who requires medical supervision. It is estimated that there was possibly an average of 5,300,000 persons who were disabled for longer than three months in 1950. These persons constituted 3.5% of the total population. Of these, about 4,200,000 were at home, and 2,120,000 were 65 or older. It would be beneficial to know how many of these could be rehabilitated to the point of reasonable self-sufficiency. The patient should be able to provide himself with the basic needs of food, shelter, and clothing. Those who can reach this level of self-sufficiency will give the greatest reward for the cost and effort involved.

On the other extreme we number those whose condition is irreversible. For these, mostly psychotic, paralyzed, arthritic, tuberculous, deaf, blind, or feeble-minded, domiciliary care under institutional supervision seems the best that can be done. The Commission discusses what should constitute minimal acceptable care and attention and applies this ideal as the minimum for everyone. One can agree to this ideal while questioning its practicability. To build and equip the facilities and to train the nurses and 35 kinds of technical personnel required—the services of one or more of which will be needed during the course of chronic illness—is beyond the fiscal capacity of private charity or the taxpayer. Taxes from local, state, and federal governments already take about 33% of earnings. The only reference to a fiscal plan to implement the Commission's recommendations appears on page 441 (paragraph 69-b):

> Until the time when the needs of all long term patients are adequately met under plans and programs listed here, there is no alternative to the basic proposition that society as a whole through taxation must meet the deficit and fill the gap. Funds for this purpose should be provided by local, state and federal taxation. Medical care of the long term patient currently is financed in a variety of ways: through direct personal financing, voluntary health insurance, philanthropic agencies, workmen's compensation, non-occupational disability insurance, industrial medical care programs and tax funds.

The authors are to be commended for their thorough explanation of the many factors involved. They have defined long-term patients and subdivided this group according to dominant causative characteristics. This breakdown indicates which of these persons can be rehabilitated in whole or in part. They are the ones for whom the expenditure of more funds can be justified from the standpoint of economy. The long-term patient who can be returned to productive living ceases to be a long-term expense.

**Biochemical Individuality: The Basis for the Genetotrophic Concept.** By Roger J. Williams, Professor of Chemistry, Director, Biochemical Institute, University of Texas, Austin. Cloth. $5.75. Pp. 214, with 17 illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W.C.2, England, 1956.

In this volume the author stresses the importance of the uniqueness of the individual as opposed to the similarity between individuals. If one considers the wide variations existing in many clinical values in the so-called normal person, it becomes readily apparent that, when extremes are persistent in normal persons, these individuals differ profoundly even though clinical values are within the normal. Such differences are not surprising when one considers the numerous enzymatic reactions controlling body functions and the results when several of these reactions are functioning other than optimally.

The first two chapters may be considered introductory, in that the author establishes the significance of biochemical variation and the basis for biochemical individuality. The next eight chapters point out areas of existing individuality in anatomy, chemical composition of the body, enzyme patterns, endocrine activity, excretion patterns, drug response, and nutrition. The latter area includes a discussion on the amounts of inorganic and organic constituents present in the body and the quantities of each required by individuals. A single chapter containing a miscellaneous group of areas of individuality is also included. In chapter 11 the author explains the genetotrophic concept as based on biochemical individuality. The principle simply stated by the author is: "Every individual organism that has a distinctive genetic background has distinctive nutritional needs which must be met for optimal well-being." The final three chapters contain ideas with respect to the implications this concept has in the biological sciences, medicine, dentistry, and psychiatry. The book makes interesting reading because of the freshness of the concept it contains and the immense areas it opens in both fundamental and applied research. It contains pertinent technical references at the end of each chapter and a general subject index.

**Training of the Lower Extremity Amputee.** By Donald Kerr, B.B.A., Director, National Institute for Amputee Rehabilitation, Lodi, N. J., and Signe Brunnstrom, M.A., Consultant in Amputee Training, Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, New York. Introduction by T. Campbell Thompson, M.D. Cloth. $6.50. Pp. 272, with 153 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1956.

Donald Kerr, himself an above-knee, lower extremity amputee, and the co-author state that their reasons for preparing this book were to inform the surgeon about rehabilitation of the amputee, to inform the nurse on stump care, to give the physical therapist a program of preprosthetic care and techniques for training the amputee, to inform the limb maker about stump care and training techniques, and to instruct the amputee in preprosthetic care, selection and testing of the prosthesis, and exercises in its use. The book is well illustrated. Its 12 chapters are entitled (1) Adjusting to the Amputation, (2) Pre-prosthetic Period, (3) Lower Extremity Prostheses, (4) Stump Socks and Dressing Hints, (5) The Single Above-Knee Amputee: Training, (6) The Single Above-Knee Amputee: Walking, (7) The Single Above-Knee Amputee: Daily Activities, (8) The "Tilting Table" Amputee: Training Methods, (9) The Single and Double Below-Knee Amputee: Training Methods, (10) The Double (One Above and One Below-Knee) Amputee: Training Methods, (11) The Double Above-Knee Amputee: Training Methods, and (12) Social Dancing and

Sports. The book is well printed and adequately indexed. The authors give a practical description of the methods used in training lower extremity amputees. This book should be of real value and interest to all physicians and therapists concerned with the training of amputees. It is highly recommended.

**The Physician-Writer's Book: Tricks of the Trade of Medical Writing.** By Richard M. Hewitt, A.M., M.D., Senior Consultant, Section of Publications, Mayo Clinic, Rochester, Minn. Cloth. $9. Pp. 415, with 37 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1957.

This book, in the words of the author, is designed "to aid the inexperienced, inexpert, occasional physician-author, whose material is written for other physicians." It is well suited for this purpose and is equally well designed to be of great service to the more experienced medical writer. The book serves as a manual of medical writing from the rules of sentence structure to the mechanics of preparing a manuscript. Every subdivision of the subject is presented in the modest, authoritative manner that is characteristic of the author.

Such practical discussions as those concerned with sources of assistance to the author, the subdivisions and organization of the article, tests of quality, paragraph structure, medical slang, tact and ethics, and the use of tables and illustrations will be of value to anyone who feels he has medical information to impart. Hewitt is not dogmatic and is not a perfectionist in the use of English. His principal interest is that the physician-author shall have expressed himself in reasonably good English but in a manner which is pleasing to the reader and capable of no misunderstanding. His book is superior to any previous one on the subject. Its superiority springs from the fact that the author was a teacher of English before he turned to the study of medicine. To this background is added some 25 years of writing and editing while employed by the American Medical Association and the Mayo Clinic. His book is highly recommended.

**Orthopaedic Nursing.** By Mary Powell, S.R.N., M.C.S.P., Matron, Nuffield Orthopaedic Centre (Wingfield Morris Orthopaedic Hospital), Oxford. Foreword by Sir Reginald Watson-Jones, B.Sc., M.Ch. Orth., F.R.C.S., Extra-Orthopaedic Surgeon to Her Majesty the Queen. Second edition. Cloth. $6. Pp. 440, with 271 illustrations. E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland; [Williams & Wilkins Company, Mount Royal and Guilford Ave., Baltimore 2], 1956.

This book contains much information which should be of interest and help to the nurse who wishes to become proficient in the care of orthopedic patients. A large portion of it deals with the care of crippled children. There are great differences between the orthopedic hospital wards in England and those in the United States. In the 1920's our orthopedic hospitals were filled with patients with tuberculosis of the bones and joints and chronic osteomyelitis with multiple draining sinuses. In the United States we now rarely see a patient with bone and joint tuberculosis and still fewer patients with multiple foci of osteomyelitis. Our orthopedic nurses would be startled to see the chapters in this textbook dealing with tuberculosis of the bones and joints.

The chapter on plaster-of-paris technique, including the daily nursing care of patients who are in plaster casts, is excellent. The emphasis placed on nurse-applied physiotherapy for orthopedic patients is appropriate. This is a subject which the orthopedic nurses in the United States know little about. Chapters 24 to 28, inclusive, describe injuries to bones and joints and techniques of care of these injuries. The methods described in these chapters are timely and well presented.

**Congential Anomalies of the Viscera: Their Embryological Basis.** By J. Lewis Bremer, M.D. Cloth. $5. Pp. 202, with 89 illustrations. Harvard University Press, Cambridge 38, Mass.; Oxford University Press, Amen House, Warwick Sq., London, E.C.4, England, 1957.

The author of this book is well known for his researches on embryologic problems. While many outstanding textbooks in embryology have become available in recent years for medical students, the author, with the practitioner in mind, has recognized the need for an up-to-date volume providing concise descriptions of the more prevalent anomalies of the viscera. He has wisely stressed basic principles of developmental anatomy, for he recognizes that a basic knowledge of these will facilitate a greater interest in the more practical aspects of the subject. The anomalies, themselves, are presented with clarity and, in most instances, with the proper emphasis on those most commonly seen in practice. It might appear that the extensive account relating to interatrial septal defects and the embryology concerned has been somewhat overemphasized at the expense of that part dealing with interventricular septal defects in the section of the book dealing with septation. Nevertheless, in most instances, a wise and useful selection of illustrative material has been made. The author has succeeded in providing a book that can be highly recommended for the average practitioner, pediatrician, and internist, and he has made available a work which should be stimulating and of reference value to the medical student.

**Fundamentals of Clinical Neurophysiology.** By Paul O. Chatfield, M.D. Cloth. $8.50. Pp. 392, with 152 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1957.

In this book, based on lectures given to first-year medical students at the Harvard Medical School, the better-established facts in neurophysiology are presented in a clear, integrated manner by a qualified, experienced teacher. The text is carefully written, adequately illustrated, and soundly documented. Students, both beginners and those more advanced, should find this work accurate and informative; physicians should be enlightened concerning the basic physiological mechanisms behind the emotions, epilepsy, labyrinthine disease, sleep, sexual physiology, and similar topics. Author and publisher have coordinated their efforts to produce an outstanding book in the field.

# QUERIES AND MINOR NOTES

## ANDROGEN-ESTROGEN THERAPY FOR ELDERLY PATIENTS

To the Editor:—*An editorial in* The Journal *(163:359 [Feb. 2] 1957) discussed the proportion of estrogens to androgens in hormone therapy for elderly patients. Please discuss how the proportion of 1:20 was determined.*

*Robert J. Mearin, M.D., Montclair, N. J.*

Answer:—The exact amounts of androgens and of estrogens and the proper proportions of androgens to estrogens which are useful and proper in the treatment of elderly patients cannot be completely defined. There are various considerations which prevent complete exactitude. In the first place, various androgens and various estrogens differ greatly in their potency, as measured biologically per milligram of hormone injected intramuscularly. When administered orally, certain forms of androgen and certain forms of estrogen seem to be more completely absorbed and more effective than others. Another consideration is whether the combined hormone treatment is used on a male or a female patient. In general, a proportion with a larger amount of androgen is considered better for men, and a proportion supplying a larger amount of estrogen is considered better for women.

A proportion of 1:20 refers particularly to combined therapy with estradiol benzoate and testosterone propionate injected intramuscularly, since this form of combined therapy is probably the one that has been most completely evaluated.

Oral therapy employing ethinyl estradiol combined with methyltestosterone or estrone combined with methyltestosterone has also proved to be quite effective. Because of the different potencies of the various hormones concerned, the proportions in the various preparations available vary from the 1:20 cited for the intramuscularly injected hormones above. Other orally effective estrogens, such as diethylstilbestrol and dienestrol, have been combined with methyltestosterone. Estradiol combined with testosterone or methyltestosterone is said to be effective when administered in combined form by the transmucosal route. The proportion usually employed by this route is 1 mg. of estradiol to 10 mg. of methyltestosterone. When diethylstilbestrol and methyltestosterone are administered by mouth, the proportion usually employed is 1:20. Because of the very high potency of ethinyl estradiol, the proportion of ethinyl estradiol to methyltestosterone usually employed for transmucosal or oral therapy is 1:200.

Properly controlled, long-term, combined hormone therapy can be highly beneficial to elderly patients of either sex. Women patients receiving such treatment must be carefully observed to be sure that undesirable androgenic effects are not caused. Particular care must be exerted to see that excessive storage of salt and water or undesirable elevation of the blood pressure do not occur. Estrogens are the hormones most often implicated in excess fluid retention. In men, as well as in elderly women, there may be undesirable swelling and tenderness of the breasts as a result of estrogen treatment.

In women, the dosage of estrogen should be kept below levels causing uterine hypertrophy or bleeding. Also, in women the appearance of acne, excessive hair growth on the face and body, deepening of the voice, or hypertrophy of the clitoris may indicate excessive androgen effect. It is much better not to adhere too closely to any numerical ratio between estrogens and androgens but to adjust the treatment and the dosages of the hormones according to the objectives desired and the results obtained.

## TREATMENT OF CHOLELITHIASIS IN EXTREMELY OBESE PATIENT

To the Editor:—*A patient weighs 305 lb. (138.3 kg.) and has a blood pressure of 280/152 mm. Hg. Blood sugar level and basal metabolism rate are normal. Her gallbladder is full of stones, which give her symptoms. She has been receiving 0.25 mg. of Serpasil twice a day and has been on a low-calorie diet. She is also receiving Biphetacel to control her appetite. Please advise as to treatment of this patient.*

*G. K. Mahl, M.D., Ironton, Ohio.*

Answer.—The patient described has extreme obesity, severe hypertension, and cholelithiasis. All of these conditions require treatment, and they may be interrelated. Since the gallstones are causing symptoms, plans should be directed toward getting the patient in condition for cholecystectomy. However, the cholecystectomy should be postponed, if possible, until weight reduction has been accomplished and until the blood pressure has been brought under control. Weight reduction should be slow but steady, with a diet allowing 1,000 to 1,200 calories daily, depending on the activity of the patient. If possible, she should be moderately active physically. Strenuous exertion must be avoided because of the extreme obesity and the hypertension. Walking on the level or similar exercise should be beneficial. Amphetamine in various forms may reduce appetite without increasing the blood pressure. Some of the slowly absorbed forms may be given in a single dose before breakfast, or, if this is not adequate, another dose should be given one-half to one hour before lunch and before supper. The basal metabolic rate is reported as normal, but this should be checked by protein-bound iodine and blood cholesterol determinations. If the blood protein-bound iodine

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

level is within normal limits, thyroid therapy is not indicated. If, however, the blood cholesterol level is high and the protein-bound iodine level is low, thyroid in proper doses to bring the basal metabolism rate to normal may be indicated. Weight reduction should assist greatly in returning the blood pressure toward normal. Use of the various types of ganglionic blocking agents, such as pentolinium and hexamethonium compounds, should be reserved and employed only if weight reduction and other measures are not successful in bringing down blood pressure.

X-ray study of the skull to rule out possible lesion in the hypothalamus or pituitary region should be done. Emphasis should be placed upon providing an attractive and prolonged weight-reduction program through dieting. Lean meat and other protein foods should be taken in fairly generous amounts. Bulky foods, such as salads, fruits, and vegetables, should be provided generously. Sweets, starches, and fats, in general, will have to be greatly curtailed. Bread, preferably as whole wheat bread, one slice at a meal, is allowed. A multiple vitamin capsule will insure adequate vitamin intake. Psychological factors should be investigated. Frequently the cause of excessive caloric intake over a long period of time is psychological. Pleasure in eating may become a dominant personality trait and may serve as a substitute when social, business, or sexual desires are unsatisfied. Obesity itself may be used as a weapon against undesired demands of work, family, or community. Corpulence may serve as a guard against frustrations resulting from loss of physical attractiveness and efficiency. Problem children often become obese and use the condition to demand special attention. In a great majority of cases of obesity both physiological and psychological abnormalities are factors in causation of the obese condition. Individual study in each case is necessary to discover the causes, which are usually multiple.

## ALLERGIC DERMATITIS IN A MEAT PACKER

To the Editor:—*A 32-year-old woman who has been wrapping meat for five years in a chain grocery developed an eczematoid dermatitis, obviously of an allergic nature, on the ventral surface of both arms (she works in a short-sleeved uniform) and on the neck and upper part of the thorax. The eruption is macular and bright reddish at its height; on one occasion it progressed to a weeping stage. Antihistamines and cortisone cause prompt remissions, but when she returns to work the process begins again after about one week. Itching is present. The wrapping of meat entails the use of cellophane paper. When the paper is folded around the meat and creased, the operator irons it with a hot iron. This produces a sealing of the paper and also produces a smoke that envelopes the operator. Incidentally, there is an almost constant "sore throat." Is this patient reacting to the fumes produced by this process on these papers?*

*Benjamin L. Camp, M.D., Atlanta, Ga.*

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—It is impossible to diagnose a dermatitis from a description and a history. However, the concept that the dermatitis in this patient might be due to an external contact seems reasonable. Furthermore, the idea that it might be due to exposure to a chemical or a fume is suggested by the distribution of the eruption and the history of exacerbations on return to work. However, to establish the cause, patch tests would be necessary. Contact dermatitis is not common in meat wrappers. Eruptions due to cellophane are also unusual. Cellophane is used in performing patch tests because it is nonirritating. It is desirable to have a clear area, free from dermatitis, between the tape, which is so often irritating, and the tested substance. Cellophane is ideal for this purpose. Reports of cellophane toxicity could not be found in the available literature, except that Hunter (Diseases of Occupations, Boston, Little, Brown & Company, 1955) quotes an inconclusive personal communication from Flinn (1943), who claimed to have produced paralysis of the wings and legs of domestic fowl fed cellophane for 28 days. Schwartz, Tulipan, and Peck (Occupational Diseases of Skin, ed. 2, Philadelphia, Lea & Febiger, 1947, p. 525) state that industrial dermatitis does not occur in cellophane workers. It must be admitted that sensitization could develop to the fumes emanating from the heated cellophane. However, the physician must consider other possible causes, such as plants, insecticides, other chemicals, detergents and photosensitization. Despite the suggestive history, the actual cause may have nothing to do with her task of wrapping meat. Other substances in her vicinity or agents contacted away from work might be at fault. Therefore, it must be reiterated that careful patch test studies on this patient to determine the exact cause is imperative before a definite decision can be rendered. If patch tests with the cellophane used in her work are negative at normal temperatures, controlled exposure to the fumes should be attempted. It might be worth mentioning that this consultant has seen a similar case in which the actual cause was found to be sensitivity to external contact with beef. Another possibility to be considered would be that the patient is not using cellophane but is exposed to another similar product containing sensitizing chemicals. This should be checked with the manufacturer.

Answer.—It may be doubted that cellophane itself may be the source of the conditions described. There is the remote prospect that some plasticizer or moisture-proof agent when added could induce the affections. This must be tested through the application of appropriately applied closed skin patch tests. In some such tests, when allergy is suspected, the material should be kept in place for longer than customary periods and up to 96 hours. This being true, several samples of the mentioned materials should be applied in order that one may be removed at the end of 8, 24, 48, and 96 hours. The test materials should include cellophanes as such, but other tests should make use of the same items applied promptly after more heating than is required in the work operation. Likewise, these samples should be removed at dif-

ferent periods up to 96 hours unless earlier-removed patches indicate positive responses. Wholly negative results should go far in exculpating cellophane as the offender. A common source of dermatitis in butchers, and notably fish butchers, is the erysipeloid organism Erysipelothrix rhusiopathiae. The cleaning agents utilized around meat blocks and counters are a more likely source of dermatitis than cellophane.

## PREGNANCY IN PRESENCE OF MYOMAS

To the Editor:—*A 32-year-old married woman has been having intermittent functional bleeding for the past six months. This has been somewhat worse lately. A careful dilatation and curettage was done five months ago, and a cervical polupus was removed. The patient has multiple small fibroid tumors of the uterus that can be palpated through the abdominal wall. She has a mild mastitis, especially in the left breast, which is sore around her menstrual time. She has been married only a short time, and she wishes to have children. Should the patient be allowed to become pregnant, or should a hysterectomy be done, with complete removal of the fibroid tumors? Although the tumors are small, there is still the problem of functional bleeding. A roentgenologist strongly advises against x-ray therapy in view of recent knowledge of the possibility of mutations in the second generation.*

*Hamlin B. Lindsay, M.D., Washington, Ind.*

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—The patient poses several different problems, and additional information would be of value. It would be well to know how long she has been married and the histology of the specimens removed by curettage. The chief problem seems to be uterine bleeding, and the question of fertility is unanswered. It is to be hoped that the patient might get pregnant without operation, and she could probably go to term. Any operation undertaken should have as its objective the possible relief of bleeding, without interfering with the possibility of pregnancy. The possibility of myomectomy immediately suggests itself if the bleeding is debilitating or if the tumors are growing rapidly. It is possible to remove many fibromyomas, including submucous, and preserve a uterus that is capable of impregnation and maintaining pregnancy. With tumors, especially submucous, it is more likely that the bleeding is organic rather than functional. The often-associated hyperplasia of the endometrium and the possibility of adenocarcinoma with fibromyoma should be kept in mind. X-ray therapy is contraindicated in this patient. The breast complication at the menstrual time is not indicative of failure of ovulation. With definite pathology in the pelvis as described, endocrine therapy probably would not be helpful. On the basis of the information at hand, it is suggested that pregnancy be encouraged, with some assurance that if accomplished it would go to termination. If the symptom of bleeding becomes more severe, operation might be necessary; however, conservative measures should be used if possible, in the hope of preserving childbearing function. The most radical procedure would be complete hysterectomy, but it is hoped that this would not be necessary. X-ray therapy in doses large enough to cause cessation of uterine bleeding in this patient would likely produce ovarian failure and would thus eliminate any worry concerning pregnancy and mutations in the second generation.

Answer.—From the description of findings and symptoms, it would seem that hysterectomy is not necessary and that myomectomies would not be feasible. Investigation of the fertility of husband and wife should be done, followed by such treatment as may be indicated. There does not seem to be any reason that pregnancy should not be attempted.

## FUNCTIONAL GASTRIC DILATATION

To the Editor:—*A 39-year-old man suffers from periodic episodes of acute gastric dilatation. This is manifested by marked bloating and is usually accompanied by copious salivation. These attacks occur particularly when the subject is under some sort of mental strain or tension. A recently performed gastrointestinal series was negative for organic pathology. Examination of the heart, lungs, and blood pressure and serologic tests are negative. Antispasmodics and sedatives have been tried, to no avail. The patient obtains some relief by lying supine. The attacks may last up to one week and cause the patient considerable anguish. He may be perfectly normal for several months at a time and then suffer another attack. Please provide suggestions as to therapy of this apparently functional disorder.*

*M.D., New York.*

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—It is assumed that all possible organic conditions, even such uncommon conditions as diaphragmatic hernia, have been ruled out and that the patient's symptoms of acute gastric dilatation and marked salivation are functional or, more correctly speaking, psychogenic in origin. This impression is heightened by the fact that these symptoms occur intermittently and at times when the patient is under severe mental stress. It is a well-known fact that in states of acute anxiety or panic, symptoms of autonomic imbalance, such as dryness of the mouth and spasticity of abdominal viscera, are very common. In the case under discussion the symptoms presented by the patient, salivation and flaccidity (dilatation), although less commonly encountered, may also be ascribed to autonomic imbalance. The description of the attacks as presented strongly suggests an anxiety state; hence, a thorough psychiatric evaluation should be made. Every effort should be made to determine the psychodynamic factors that are responsible for this condition and then to institute the proper psychotherapeutic procedures. For symptomatic relief of the distressing physical symptoms, preparations of atropine and nicotinic acid may be tried.

ANSWER.—The description of the symptoms, periodicity of occurrence, aggravation by mental strain and tension, and relief by lying supine suggest that this patient probably suffers from aerophagia that may be associated with a cascade type of stomach. If relief is not obtained by his lying supine or in the right lateral decubitus position, it may be well to train the patient to empty his stomach with an Ewald tube in order to obtain immediate relief. He should then be instructed in regard to a bland dietary regimen, with six small feedings daily instead of the usual three large feedings. In addition to these measures, one should probably concentrate most intently on the psychotherapy of the patient and reassurance as to the functional etiology of his symptoms. The patient should be instructed in regard to the mechanism of aerophagia and encouraged to make a conscious effort to refrain from air swallowing if he is ever to obtain permanent relief from his annoying psychosomatic complaint.

## TREATMENT OF NEVI

TO THE EDITOR:—*A 50-year-old woman has been noticing a blue nevus of pinhead size on the tip of the nose and a junction nevus on her right cheek under her eye, without any changes, for about one year. She would like to have both removed for cosmetic reasons. Is it not a "must" to have the blue nevus removed as soon as possible? Why do dermatologists advise excision instead of cauterization? Would cauterization starting about 2 mm. around the blue nevus and then going toward the nevus and under it not guarantee a sealing off (by coagulation) of any passway for the possible spreading of any cells of the nevus instead of the clean-cut wound edges and have a better cosmetic effect as well? What are the probable consequences if these two nevi are not removed? Recent articles demonstrated two cases of blue nevus in which, after removal of a blue nevus by excision (by reliable surgeons), metastatic carcinomas developed in the course of two years, although the primary tumors (nevi) had not shown any changes nor malignancy at the time of operation. Please comment on these points.*

*M.D., New York.*

This inquiry has been referred to two consultants, whose respective replies follow.—ED.

ANSWER.—For the purposes of this discussion, it must be assumed that the diagnoses of "blue nevus" and "junction nevus" as given in the question are proved correct by histological examination. It is not a "must" to remove the blue nevus as soon as possible. True blue nevi are considered to be benign lesions. They are not premalignant. Melanomatous degeneration in such growths is very uncommon. Characteristically, malignant melanomas develop in junction nevi. The latter type of tumor should be removed completely as soon as possible if it is subjected to trauma. However, most junction nevi do not undergo malignant degeneration during the lifetime of the patient. Therefore, there is a disagreement as to whether all junction nevi should be removed. This decision must be made in individual cases by the clinician in charge of the patient or by his consultants.

The type of cauterization of premalignant nevi that is condemned by dermatologists, surgeons, and pathologists refers to chemical or electrical destruction of the lesion with acid or by electrodesiccation. Usually, such destruction is incomplete. It is possible that this trauma is apt to increase the malignant tendencies of the remaining viable tumor cells. Recent unpublished studies by Walton throw some doubt on this thesis. However, until his experiments are confirmed by others and followed for a longer period of time and in larger series, it would be safer to assume that incomplete removal is dangerous. With microscopic control, as advocated by Mohs, chemical destruction is permissible. Excision is a more certain method of removing the entire tumor than the type of cauterization mentioned above and is preferred for melanomatous or premelanomatous neoplasms. The excision of such a growth with a cutting cautery is another matter. This is an excellent method of treating such a new growth. Theoretically, the sealing of blood vessels and lymphatics by such a method is advantageous. However, this advantage is more apparent than real. If the nevus is removed completely by scalpel excision and the wound sutured, there should be no nevus cells left to become malignant or to metastasize to other portions of the body. The only objections to cautery excision would concern comparatively erratic scarring and slow healing. Such treatment might well result in a disfiguring scar on the tip of the nose in comparison to the result with scalpel excision and suturing or grafting. In all probability, failure to remove these nevi would result in no harm to the patient. However, if the junction nevus shows activity in the form of growth or darkening of color, excision is advisable. Certainly, neither lesion described in the question would seem to be in areas subjected to excessive trauma. It must be emphasized that incomplete removal, with too much attention paid to cosmetic considerations, would be more dangerous than therapeutic inactivity.

Melanomas may metastasize widely before there is clinical or histological evidence of malignant activity in the supposed primary lesion. However, there are certain reservations to the glib acceptance of these cases as being proved. Unless serial sections are studied, one might miss microscopic changes of malignant activity that could be overlooked in sections taken haphazardly from different levels of the block. Secondly, even a postmortem study might fail to uncover a primary malignant melanoma in some other part of the skin, central nervous system, eye, or mucous membranes. Therefore, one can understand that the removal of a nevus considered to be benign on histopathological examination does not preclude the possibility of a focus of malignancy somewhere in that neoplasm nor that the patient may not have a comparatively hidden primary melanoma elsewhere in his body. As stated previously, ordinary blue nevi are benign and do not metastasize. The cellular blue nevus of Allen may metastasize to lymph nodes, but this is a different tumor from the true blue nevus.

ANSWER.—A pinhead-sized area of pigmentation remaining unchanged for a period of one year is not at all characteristic of a true pigmented nevus. In a woman of 50 years of age, it is much more likely that what is described is a very minute area of early senile lentigo or freckle. The true nevus is not ordinarily of this dimension. It is hardly likely that upon pathological examination neval cells will be found. The blue nevus is ordinarily the pigmented (Jadassohn-Tierche) type of nevus. This is almost always a benign growth.

## NOCTURNAL PAIN WITH RHEUMATIC FEVER

TO THE EDITOR:—*A 21-year-old man has a history of six episodes of acute rheumatic fever between the ages of 11 and 19. The physical, x-ray, and fluoroscopic examinations reveal that the patient has a combined mitral and aortic lesion and that the lesion in both valves is predominently one of insufficiency. His heart is very enlarged, especially on the right side. The cardiac rhythm and rate are normal, and the aorta is relatively small. Blood pressure in the right arm is 172/0 mm. Hg. His lungs are clear, but his liver is enlarged about three fingerbreadths below the costal margin and is slightly tender. At the present time the patient's chief complaint is that he gets a sharp pain just under the xiphoid process almost regularly at midnight and only sometimes during the day. This pain lasts about one and one-half to two hours and is not associated with eating. He has no cough, hemoptysis, or edema. What is the possible cause of "midnight pain" in this patient, and what therapy would bring relief? Antispasmodics and sedatives, such as Belladenal Spacetabs, Dactil, Tridal, and Spastosed, do not help too much. A consultant feels that, because of severe involvement of mitral and aortic valves, this patient is not a suitable candidate for surgical treatment with the techniques presently available.*

*Juliann Movchan, M.D., Oakwood, Ohio.*

This inquiry has been referred to two consultants, whose respective replies follow.—ED.

ANSWER.—It is inferred from the query that the subxiphoidal distress of which the patient complains is causally related to assumption of the recumbent posture. It would be interesting to know what precipitating factors seem to be operative when similar, but apparently much less frequent and milder, discomfort occurs during the day, eg., changes in body position, exertion, or emotional stress. Possible causes of this symptom are (1) increased liver engorgement producing, especially when the patient is in the decubitus position, unusual traction on the xiphosternal ligaments and/or diaphragmatic attachments; (2) atypical angina pectoris due either to a reduction of the cardiac output with a resulting diminution of coronary blood flow or to increased pulmonary congestion and pressure secondary to an augmented pulmonary blood volume during recumbency (the pain in the latter situation, however, would be much more apt to be midsubsternal or located diffusely over the anterior chest); (3) increased right ventricular volume, secondary to increased venous return, resulting in more traction on the xiphosternal ligaments; and (4) diaphragmatic hernia.

If hiatal hernia has been ruled out, such measures as the use of digitalis, diuretics, and Decholin ought seriously to be considered. If the employment of these agents in adequate amounts has no beneficial effect, long-acting vasodilators, such as some of the newer forms of nitroglycerine, choline theophyllinate, and pentaerythritol tetranitrate, might be given a trial.

ANSWER.—In all probability, this 21-year-old man will never be a candidate for corrective surgery. The recurrent episodes of acute rheumatic fever, the last occurring two years ago, and the findings of far-advanced valvular heart disease pose a complex problem. Disregarding the technical aspects of improving the combined aortic and mitral insufficiency, it would seem quite likely that this patient has active myocardial disease as well. The likelihood of active rheumatic myocarditis is in itself a strong deterrent to elective cardiac surgery, even though the valvular disease may be amenable to corrective surgery.

Nocturnal pain is not uncommon in young patients with severe aortic insufficiency. This is in sharp contrast to the exertional type of angina associated with aortic stenosis. This fact has been recognized for some time and is looked upon as an ominous finding from the standpoint of the patient's longevity. This pain is thought to be anginal in nature, although its nocturnal occurrence is not understood. Medical therapy is often unsatisfactory, but it would nevertheless seem advisable to try the medicaments usually employed for angina pectoris. Young adults who have a history of recurrent episodes of acute rheumatic fever and who present multivalvular lesions constitute real problems in therapy. Surgical intervention is rewarded only in those cases in which the rheumatic myocarditis has subsided. This would seem quite unlikely when there are persistent congestive manifestations and when nocturnal pain becomes a clinical feature.

## SATURATED AND UNSATURATED FATS

TO THE EDITOR:—*Some very interesting reports have appeared on cholesterol and saturated and unsaturated fats. Are there any unsaturated oils on the market?*

*M.D., Minnesota.*

ANSWER.—Evidence is accumulating that one of the factors influencing blood cholesterol is the type of fat in the diet. Scientists are currently working on the relative importance of blood cholesterol and the amount and kind of fat in the diet in relation to coronary heart disease. However, it is certainly premature to suggest that all saturated fats be eliminated from the diet, even if this were possible. The common sources of saturated fats are hydrogenated shortenings, butter, lard, and animal fat. The common sources of unsaturated fats are corn oil, cottonseed oil, peanut oil, and certain fish oils.

## TREATMENT OF TETANUS

To the Editor:—*What is the correct method to treat tetanus in the following cases? 1. A boy, aged 10 years, weight 90 lb. (40.8 kg.), received an injury out of doors from a pointed stick. The wound, which was 0.5 in. deep and 0.5 in. long, was explored and disinfected. He was given 1,500 units of tetanus antitoxin and 600,000 units of penicillin. Penicillin was given daily or every other day for 12 days. Ten days after the injury he developed mild trismus. The next day the trismus was more marked and mild opisthotonos was present. The family thought that he had had all immunizations as a baby and a booster at the age of 5 and that he had had "a shot" after an injury in 1955. 2. Another patient had injections but is not sure what they were after injuries he received 10 years ago. There is no way of finding out definitely. There is no history of known active immunization. He now has an injury where tetanus may develop. 3. The last patient is known to have received tetanus toxoid 12 years ago and again 6 years ago. The first time, he received a series of active immunization doses. He now has an injury in which tetanus may develop. In any patient, is opening the wound at the time of onset of tetanus advisable, and, if so, to what extent?*

*M.D., Michigan.*

Answer.—In reference to the first case, in which tetanus did develop, the following statements are pertinent. First, a dose of 1,500 units of tetanus antitoxin is inadequate. The literature contains numerous references to failures in prophylaxis attending the prompt administration of this amount of antitoxin. Recommendations for minimal doses of 5,000 to 10,000 units for prophylaxis may be found in medical literature. Second, parenteral administration of penicillin in adequate recommended dosage is not reliable in the prevention of tetanus. Experiments purporting to support its prophylactic action refer to its local implantation in wounds at the time of infection, and the prophylactic effects under such conditions are far from reliable (experimental studies in animals). Third, the history is vague and makes no reference to validation concerning the time of injections or verification of the contents of the inoculations. Considerable risk is entailed in acceptance of hearsay evidence concerning immunization with tetanus toxoid. In the absence of a reliable history of toxoid inoculation, complete reliance must be based on prophylaxis with adequate amounts of potent antitetanic serum in proper doses.

In reference to the second patient, the following meaningful problem exists: The nature of the injections following trauma 10 years ago is not known. Only one injection, without a background of a reliable history of administration of tetanus toxoid in either civilian or military practice, would suggest the previous employment of tetanus antitoxin, probably of equine origin. Consequently, the presence of an injury of potential tetanogenic character would validate the use of tetanus antitoxin. To achieve this purpose, an elaborately cautious approach is indicated in order to avoid both morbidity and mortality from acute anaphylactic shock secondary to previous allergic sensitization. A detailed program applicable to this purpose is contained in an article by Spaeth (*Nebraska M.J.* **41**:224, 1956).

In reference to the third patient, the following information may be applied: First, a booster injection of tetanus toxoid may be relied on as long as 10 or more years after basic immunization. In the case cited, a booster injection was given six years ago. Hence, in general, a booster injection of about 0.1 cc. of fluid tetanus toxoid, injected deep subcutaneously, is reliable prophylaxis. For general purposes, however, in order to allow for errors in measurement and administration, a dose of 0.5 cc. should be recommended. Herein lies a differentiation between the immunologically effective and the clinically reliable amount recommended. The latter accepts the element of human fallibility under average circumstances. Second, when a delay of one or more days between injury and prophylaxis supervenes, or when a quite extensive injury possibly conducive to a short incubation period is encountered, the additive security of combined toxoid-antitoxin prophylaxis may be entertained. In other words, toxoid and antitoxin may be employed. This principle applies only when the patient has had toxoid in the past. If toxoid, in adequate amount, has not been given previously, only antitoxin is to be employed.

Exploration and disinfection of wounds is an accepted procedure in prophylaxis, provided disfigurement is not entailed. The recommendations for treatment of wounds are no different for the prevention of tetanus than for the prevention of other complications of penetrating trauma. Obviously, nonmutilating removal of foreign bodies is indicated under proper circumstances. However, local procedures should be supplemented with specific prophylactic measures, i. e., administration of tetanus antitoxin or tetanus toxoid, individually or combined, as indicated by the attending circumstances. Opening of the wound at the onset of tetanus is justified only if the wound would require surgical treatment in the absence of tetanus. In other words, general surgical principles apply. Experimental evidence indicates that surgical treatment of the local lesion does not influence the course of clinically established tetanus.

## HYPERCHOLESTEREMIA

To the Editor:—*In a patient with a blood cholesterol range of 250 to 275 mg. per 100 cc., would the use of Cytellin or nicotinic acid have virtue for cholesterol control?*

*M.D., New York*

Answer.—The Journal previously published a statement of the Council on Pharmacy and Chemistry on hypercholesteremia and atherosclerosis and a monograph on the mixture of sitosterols marketed under the trade name, Cytellin (*J. A. M. A.* **160**:670-671 [Feb. 25] 1956). Cytellin may be tried as a means of reducing the level of blood cholesterol, although the evidence so far indicates that this is considered an experimental form of therapy. There is no evidence to indicate that nicotinic acid would be useful to control the level of blood cholesterol.

# RESEARCH REVIEWS

*From time to time there will be published in this section of* THE JOURNAL *brief but not necessarily complete reviews of some of the newer clinical aspects of medical research and practice. This material is gathered specifically for* THE JOURNAL.—ED.

## HEPATITIS

The sixth international symposium sponsored by the Henry Ford Hospital in Detroit was held in October, 1956. The title was "Hepatitis Frontiers." The full text of the papers and the discussions following them will be published in book form.[1] This is a brief summary of some of the topics discussed.

It is now thought, although not by all workers in this field, that two forms of viral hepatitis, infectious hepatitis and serum hepatitis, are caused by different viruses. It has been reported that the incubation period of infectious hepatitis is 15 to 40 days and of serum hepatitis, 60 to 160 days.[2] The virus that is thought to cause infectious hepatitis is referred to as virus A (I. H.) and the virus thought to cause serum hepatitis is referred to as virus B (S. H.). According to W. P. Havens Jr.,[1] Jefferson Medical College, Philadelphia, it is at present not certain whether the immunologic difference between virus A and virus B is representative of different viruses or of various strains of a single virus with antigenic differences potentiated by as yet undefined influences. He poses the question whether the family that goes to make up virus B may represent variants of virus A. I. W. McLean,[1] Detroit, reported the successful passage of agents derived from human sources.

The incidence of serum hepatitis after the use of human blood or some of its fractions has at times been considerable. Of particular importance has been the recognition of outbreaks in clinics where incompletely sterilized instruments were used in medical and dental work and where the chances of contaminations by carriers of virus were frequent.

The epidemiology of hepatitis was discussed by J. R. Paul,[1] Yale University, New Haven, Conn. J. L. Melnick,[1] of the same university, described an explosive epidemic in India and presented evidence, obtained mostly by Indian scientists, that it was water-borne. Sven Gard,[1] Karolinska Institute, Stockholm, traced an epidemic of some 600 cases of infectious hepatitis to oysters. R. L. Gauld,[1] Walter Reed Army Institute of Research, Washington, D. C., pointed to the relatively minor role played by food and water in the dissemination of the causal agents of hepatitis in the armed forces. He believes that the scattered cases of infectious hepatitis that occur in the military forces are transmitted by person-to-person contact.

To prevent serum hepatitis, practical means of sterilizing blood have been studied. F. W. Hartman,[1] G. A. LoGrippo,[1] and A. R. Kelly,[1] Henry Ford Hospital, consider beta-propiolactone a potentially useful agent for this purpose. They believe that its action is virucidal. They are now investigating whether beta-propiolactone in a concentration sufficient to sterilize whole blood may be used without deleterious effects on erythrocytes. They hold that it has many properties that make it suitable for the sterilization of plasma. They have used it to sterilize arterial homografts and bone transplants, and they have kept packaged meat preserved by a 1% solution of beta-propiolactone for one week at room temperature without mold formation.

According to these workers,[3] beta-propiolactone can be used in the preparation of vaccines in a concentration in excess of the minimal effective virucidal dose with a wide margin of safety between the complete inactivation of virus and the loss of antigenicity. It is thought to be superior to other chemical agents in the preparation of virus-inactivated vaccines and is reported to inactivate viruses completely in 10 to 15 minutes at 37 C. Its virucidal action is said to be almost instantaneous, and viruses are inactivated before beta-propiolactone undergoes complete hydrolysis. It is stable in the absence of moisture and rapidly disintegrates in aqueous solution into nontoxic products chemically related to lactic acid. During the past five years, 414 patients in Detroit [1] received 1,153 transfusions with a total of 290 liters of beta-propiolactone–treated plasma. There were no cases of serum hepatitis following these transfusions, and there was no evidence of either acute or chronic toxic effect.

Undegraded beta-propiolactone has been studied experimentally as a carcinogenic agent.[4] The conclusion reached is that there seems to be no contraindication to its use in the sterilization of blood or plasma for transfusion because of its rapid and complete disintegration into other compounds.

According to R. Murray,[5] National Institutes of Health, Bethesda, Md., it is very difficult to destroy the agent of serum hepatitis by any means; he has been unable to do so with beta-propiolactone in a concentration of 3,500 mg. per liter. This was demonstrated in human volunteers. To reduce the quantity of beta-propiolactone necessary for the complete sterilization of biological fluids, the concomitant use of ultraviolet irradiation has been discussed at various times.[6] R. T. Jordan and L. N. Kempe,[1] City of Hope Medical Research Institute, Duarte, Calif., and University of Michigan, Ann Arbor, have attempted sterilization by gamma radiation from radioactive cobalt, and J. G. Trump,[1] Massachusetts Institute of Technology, Boston, by high-energy electrons. The

storage of pooled plasma at room temperature as a means of preventing viral hepatitis has been reported by G. Allen,[1] University of Chicago.

R. F. Norris,[1] University of Pennsylvania, Philadelphia, discussed the problem of detecting asymptomatic carriers of viral hepatitis in the selection of blood donors. Although, in his opinion, hepatic function tests used thus far do not appear to be specific for liver disease or viral hepatitis, he believes that a significant number of asymptomatic carriers of viral hepatitis can be detected by employing these tests in screening. He said that measurement of serum transaminase activity may also be useful in a screening program.

In the discussion of laboratory methods in differential diagnosis, F. Wróblewski,[1] Memorial Center for Cancer and Allied Diseases, New York, referred to measurements of glutamic oxaloacetic transaminase and glutamic pyruvic transaminase. He showed that, in acute infectious and in serum hepatitis, there is an increase in both these enzymes in the serum. He said that there seems to be a close relation between the level of these serum transaminases and the clinical state of the patient, with levels reaching a peak of 10 to 100 times the normal at the time when fever, malaise, anorexia, nausea, vomiting, and hepatic tenderness are at their height. With subjective and objective improvement, there is a concomitant fall in the level of both serum transaminases. In a paper to be published,[7] he and his colleagues claim that elevations in the serum level of transaminases reflect subclinical hepatitis more sensitively than the conventional liver-function tests.

H. Ducci,[1] Santiago, Chile, referred to the use of serum aldolase and serum iron determination in the differentiation between acute and chronic types of liver disease with jaundice. He had found that patients with hepatitis showed high aldolase and serum iron values. In acute hepatitis, aldolase and bilirubin followed a parallel course, reaching normal values almost simultaneously, while the serum iron level remained elevated for a longer period. R. Ward,[1] New York University College of Medicine, New York, said that the serum phosphohexose isomerase test developed by Bodansky was useful in the detection of the disease in children before symptoms developed.

H. L. Bockus,[1] University of Pennsylvania, Philadelphia, as moderator of the round-table discussion on differential diagnosis of hepatitis, suggested that the galactose test should not be discarded and should be used in conjunction with the other tests now in favor. G. Viollier,[1] Basel, Switzerland, showed how electrophoretic blood protein patterns may be used in the differential diagnosis of liver disease. He thought that, while the changes in the blood protein patterns are not specific for liver disease, they permit conclusions as to diagnosis and prognosis.

J. L. Bollman,[1] Mayo Clinic, Rochester, Minn., said that there are now three biliary pigments known. Pigments I and II give a direct van den Bergh reaction; they are excreted in the bile and may be excreted in the urine. He believes that pigment I and bilirubin are formed outside the liver and that conversion of these two pigments to pigment II occurs only in the liver. In animals, pigment II predominated in the blood after uncomplicated obstruction of the common bile duct, which was taken to indicate that pigment I and bilirubin continued to be converted to pigment II. With continued biliary obstruction, larger amounts of pigment I appeared in the blood. In 50 patients with hepatocellular disease or obstructive jaundice, partition of the three bile pigments of their serums appeared to indicate that retention of a large portion of pigment I was associated with hepatocellular disease and that larger amounts of pigment II were retained when biliary obstruction was present.

Observations on bilirubin-protein linkages in serum and their relation to the van den Bergh reaction have been made by G. Klatskin,[8] Yale University, who has reported that the bulk of bilirubin in serum is bound to albumin, irrespective of its behavior in the van den Bergh reaction. He believes that there is no evidence that, in the breakdown of hemoglobin, globin remains attached to its prosthetic group to yield indirect-reacting bilirubin and that the two types of van den Bergh reaction are not related to differences in bilirubin-protein linkages.

### References

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